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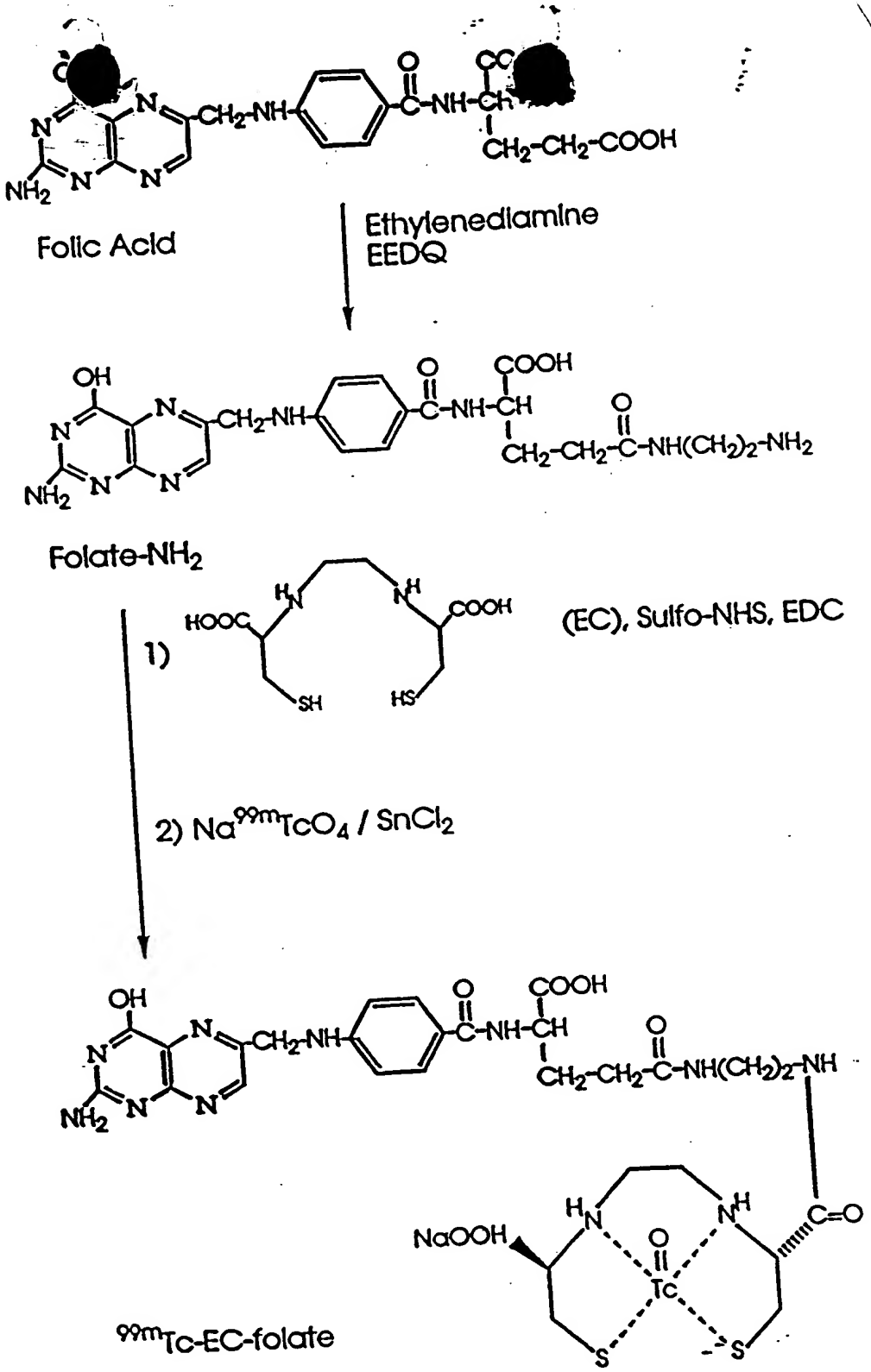

Folic Acid
Ethylenediamine
EEDQ
Folate-NH2
1)
(EC), Sulfo-NHS, EDC
2) Na99mTcO4 / SnCl2
99mTc-EC-folate

FIG. 1

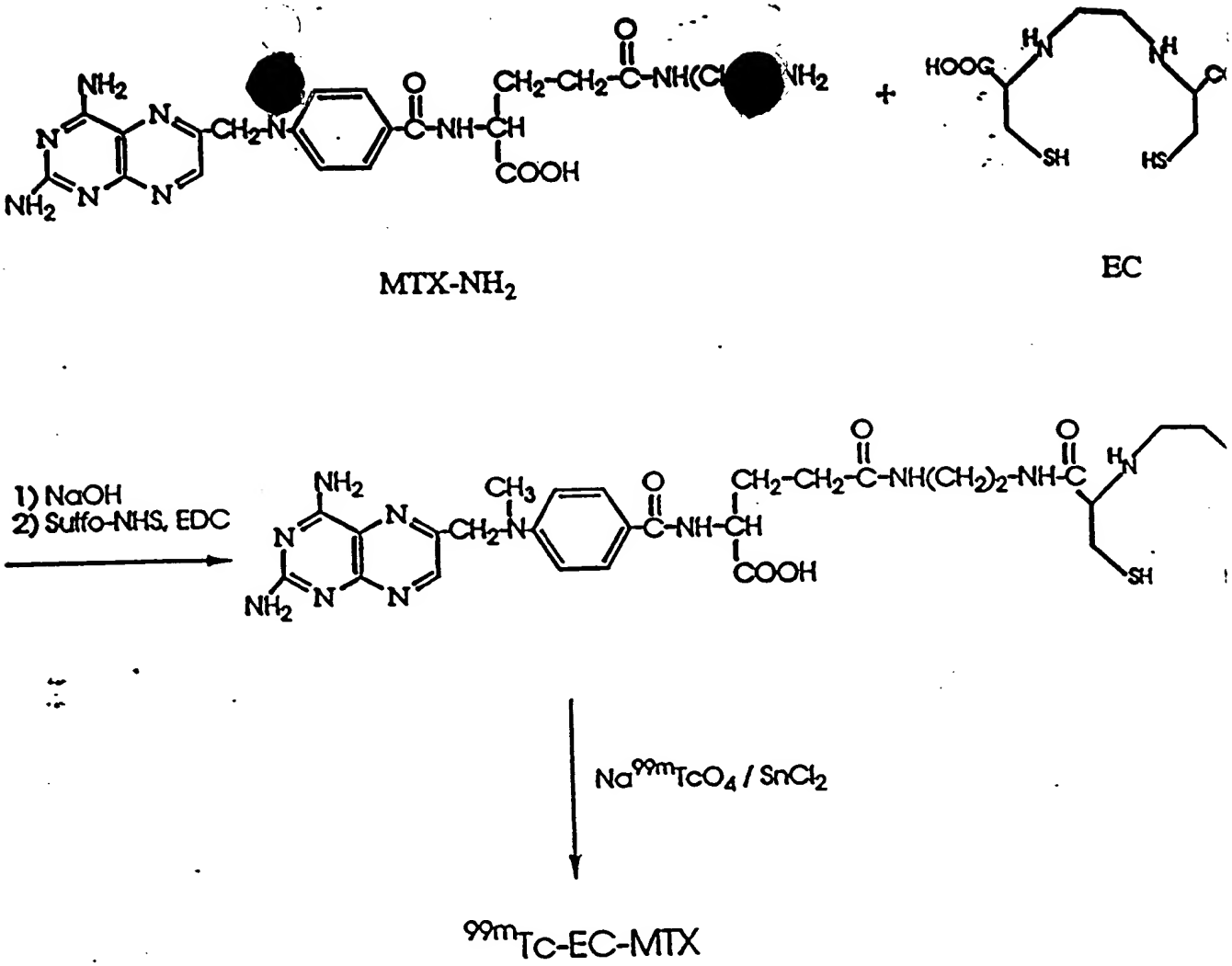


FIG 2

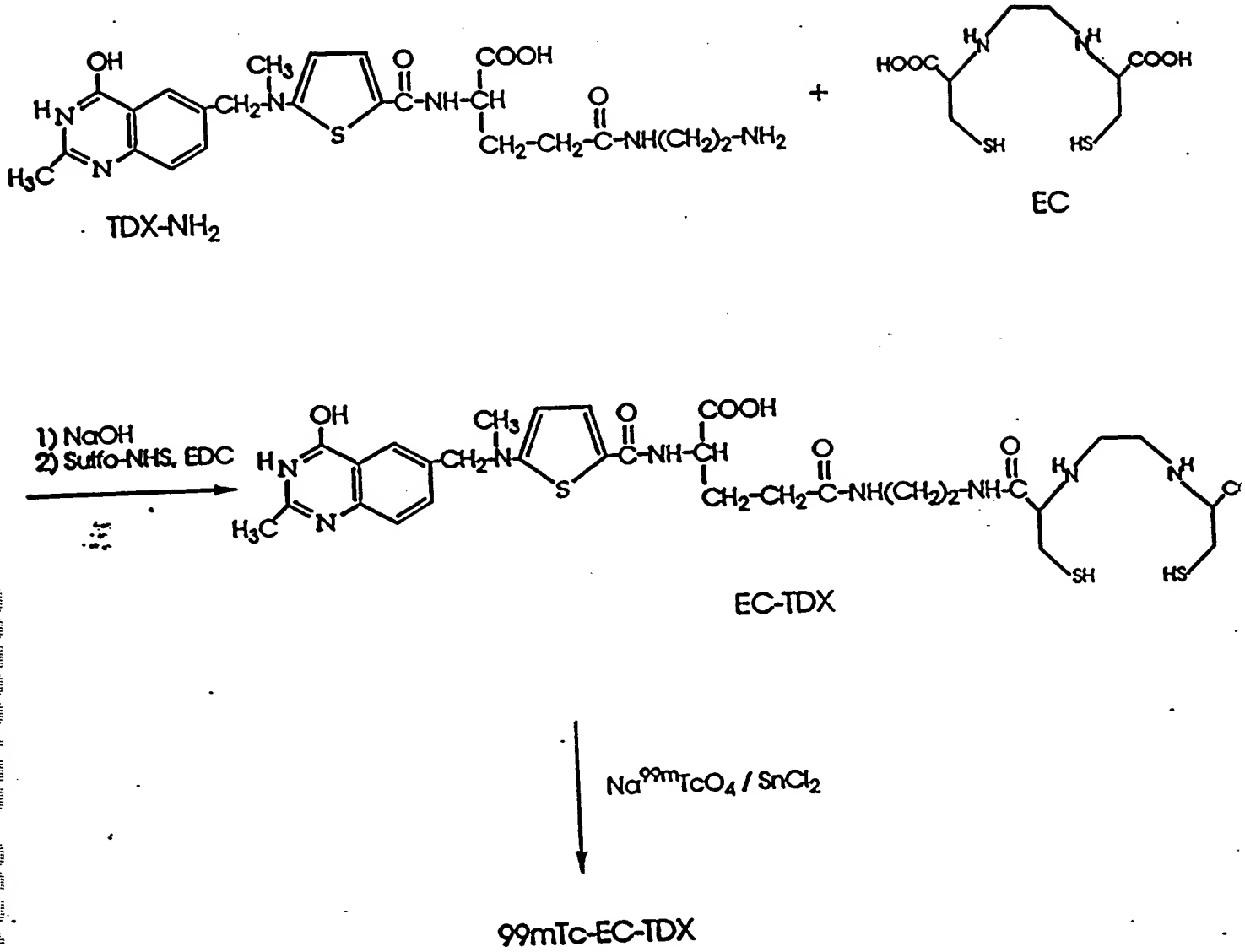

TDX-NH2
EC
1) NaOH
2) Sulfo-NHS, EDC
EC-TDX
Na99mTcO4 / SnCl2
99mTc-EC-TDX

FIG. 3

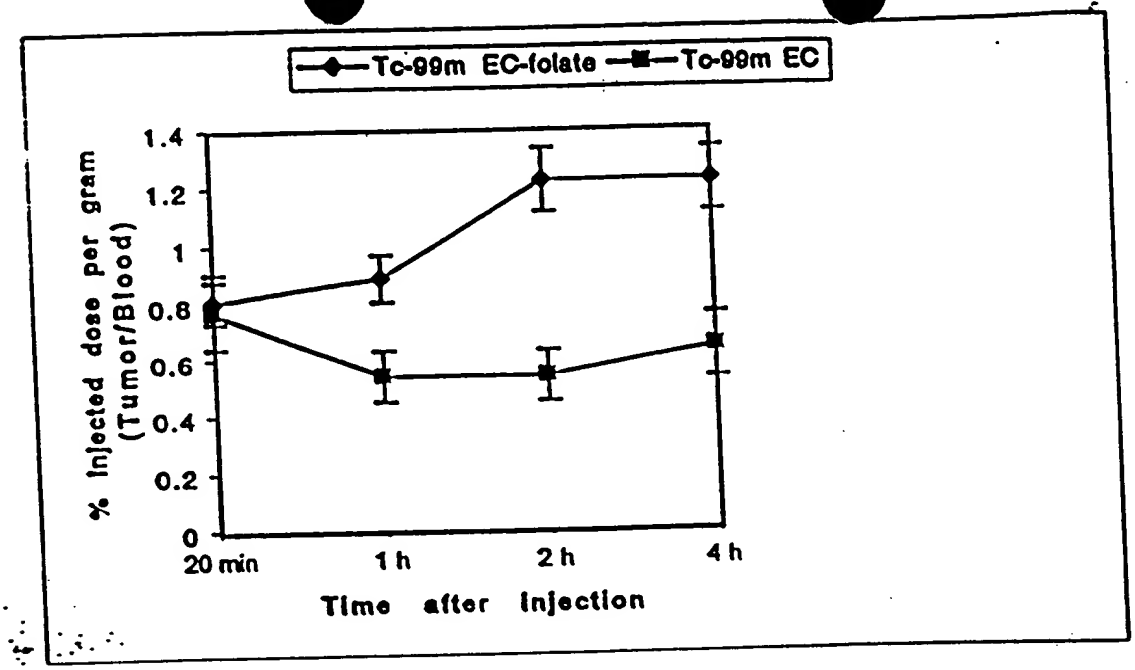

Tc-99m EC-folate
Tc-99m EC
% Injected dose per gram (Tumor/Blood)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
20 min
1 h
2 h
4 h
Time after injection

FIG. 4

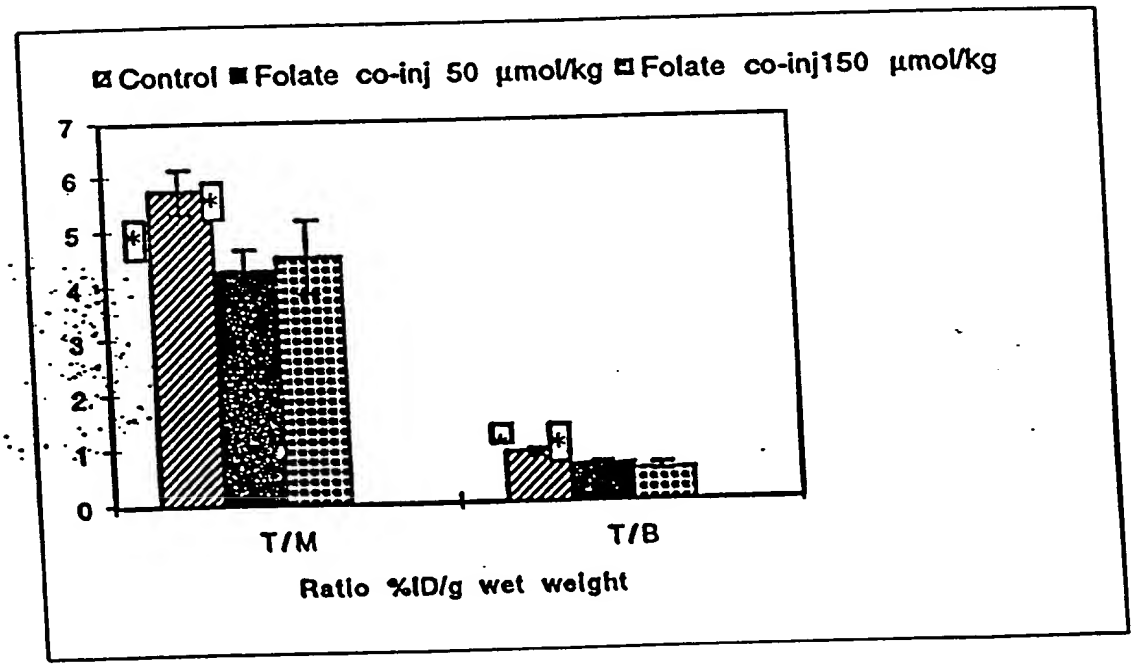

Control
Folate co-inj 50 µmol/kg
Folate co-inj150 µmol/kg
7
6
5
4
3
2
1
0
T/M
T/B
Ratio %ID/g wet weight

FIG. 5

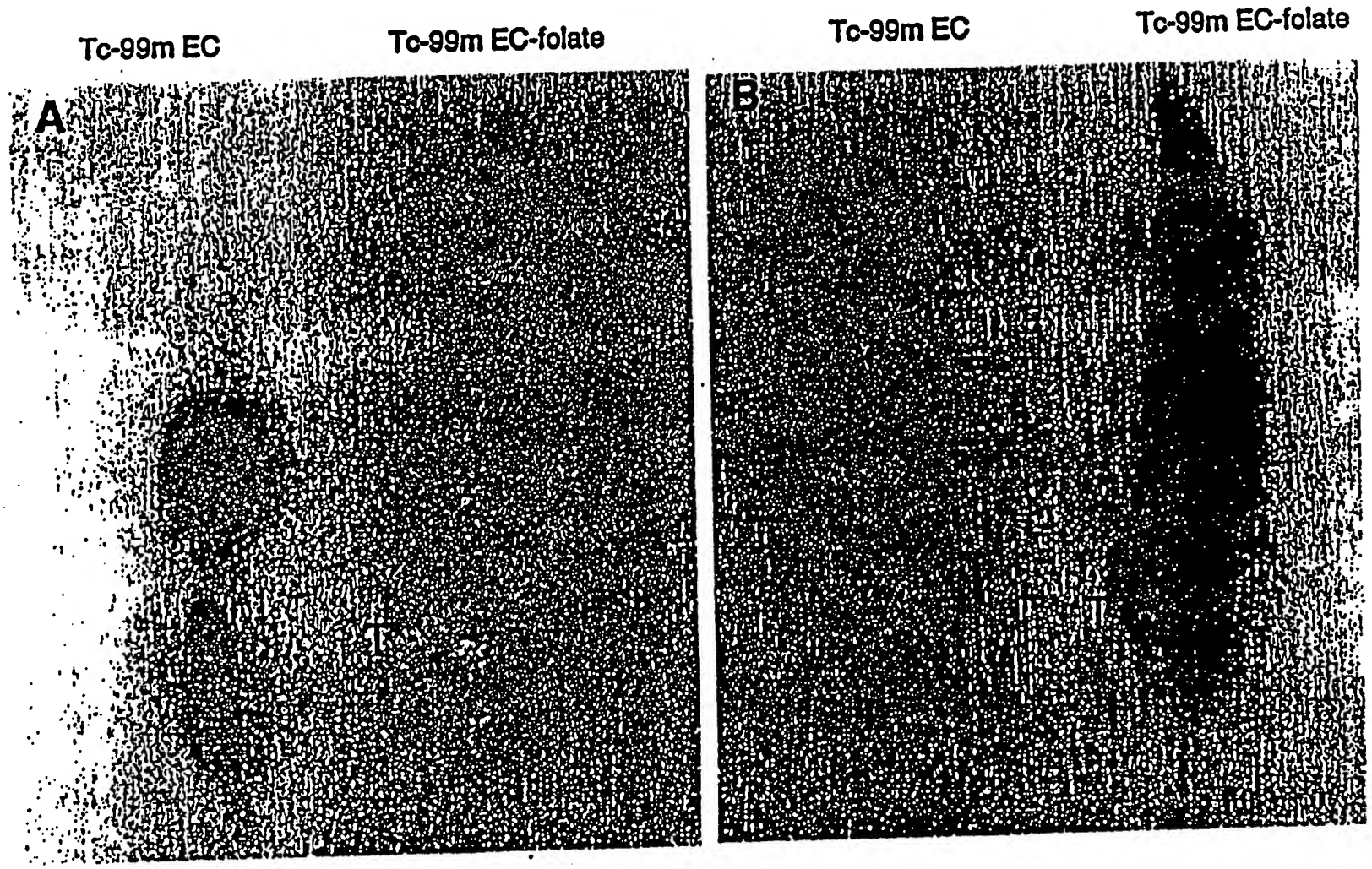


FIG. 6A

FIG. 6B

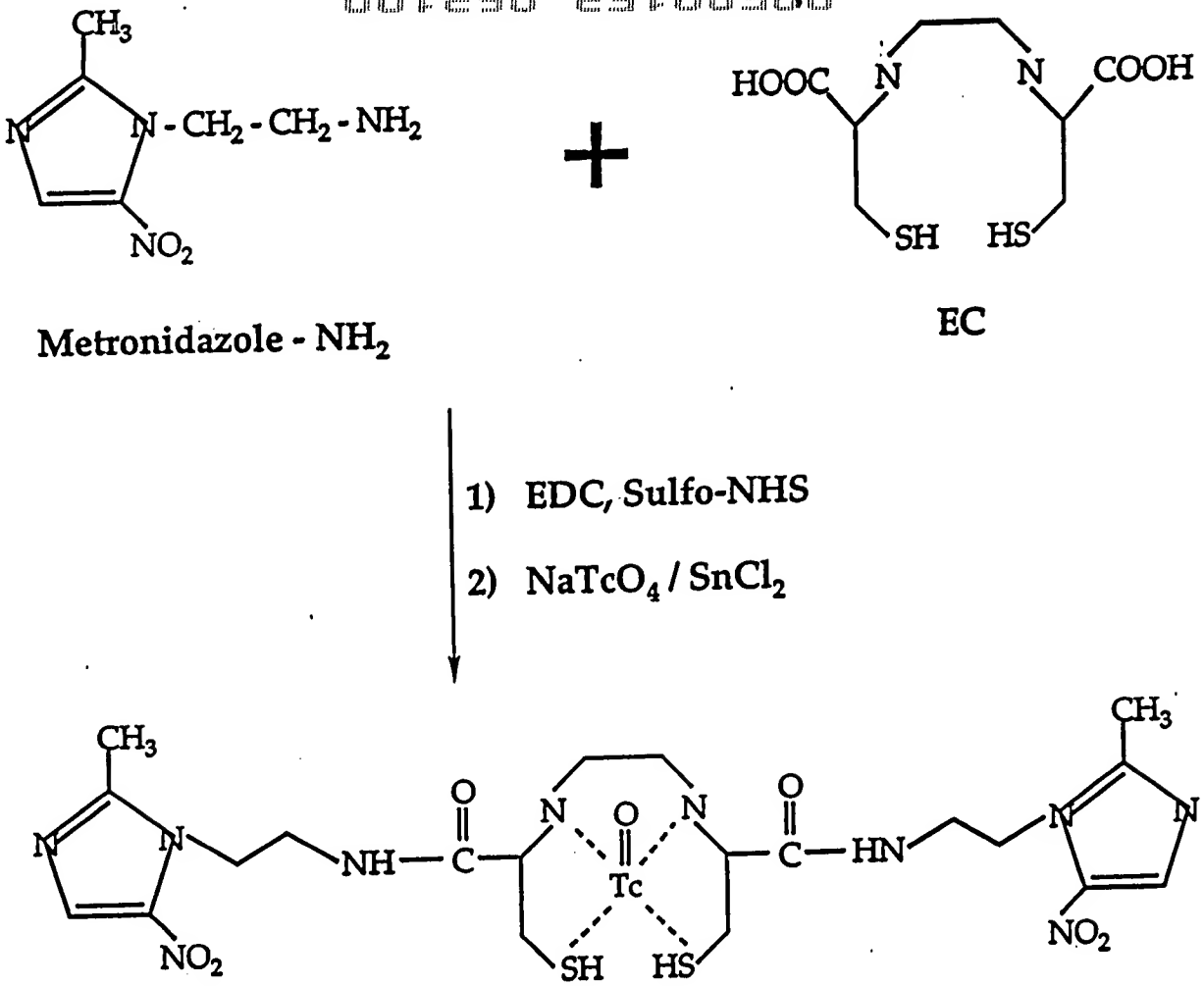
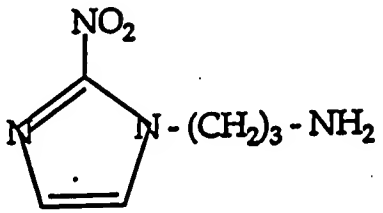
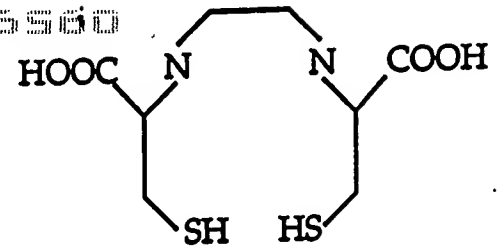


FIG. 7



2-Nitroimidazole - NH_2

+



EC

1) EDC, Sulfo-NHS

2) $NaTcO_4$ / $SnCl_2$

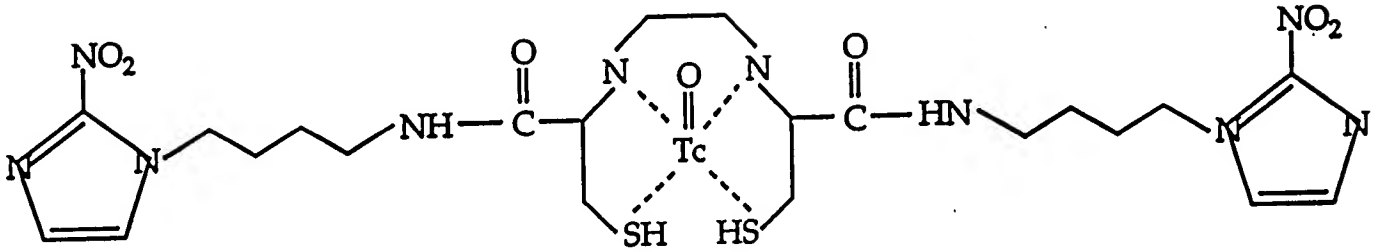


FIG. 8A

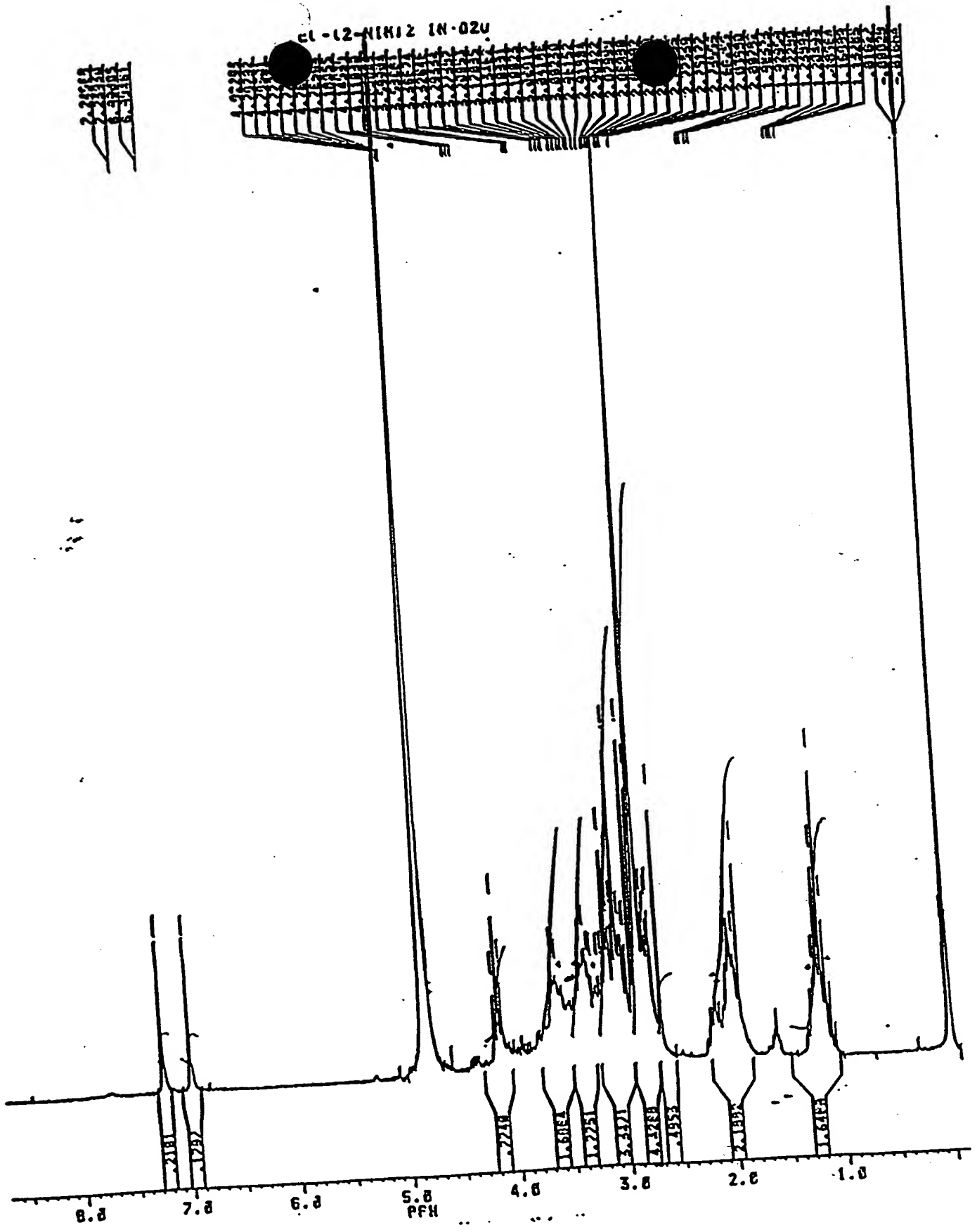


FIG. 8B

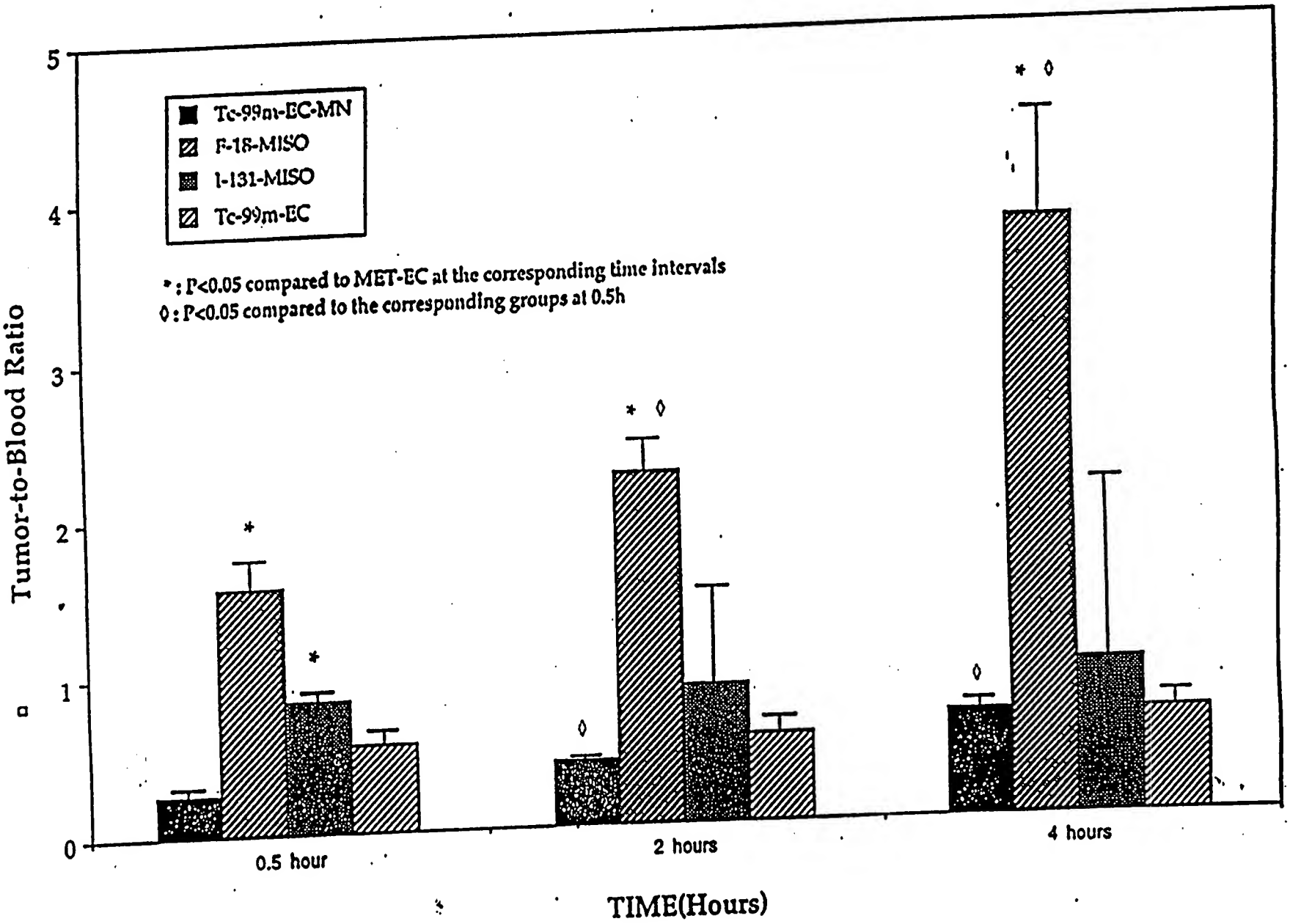

Tc-99m-EC-MN
F-18-MISO
I-131-MISO
Tc-99m-EC
*: P<0.05 compared to MET-EC at the corresponding time intervals
◊: P<0.05 compared to the corresponding groups at 0.5h
Tumor-to-Blood Ratio
0
1
2
3
4
5
0.5 hour
2 hours
4 hours
TIME(Hours)

FIG.9

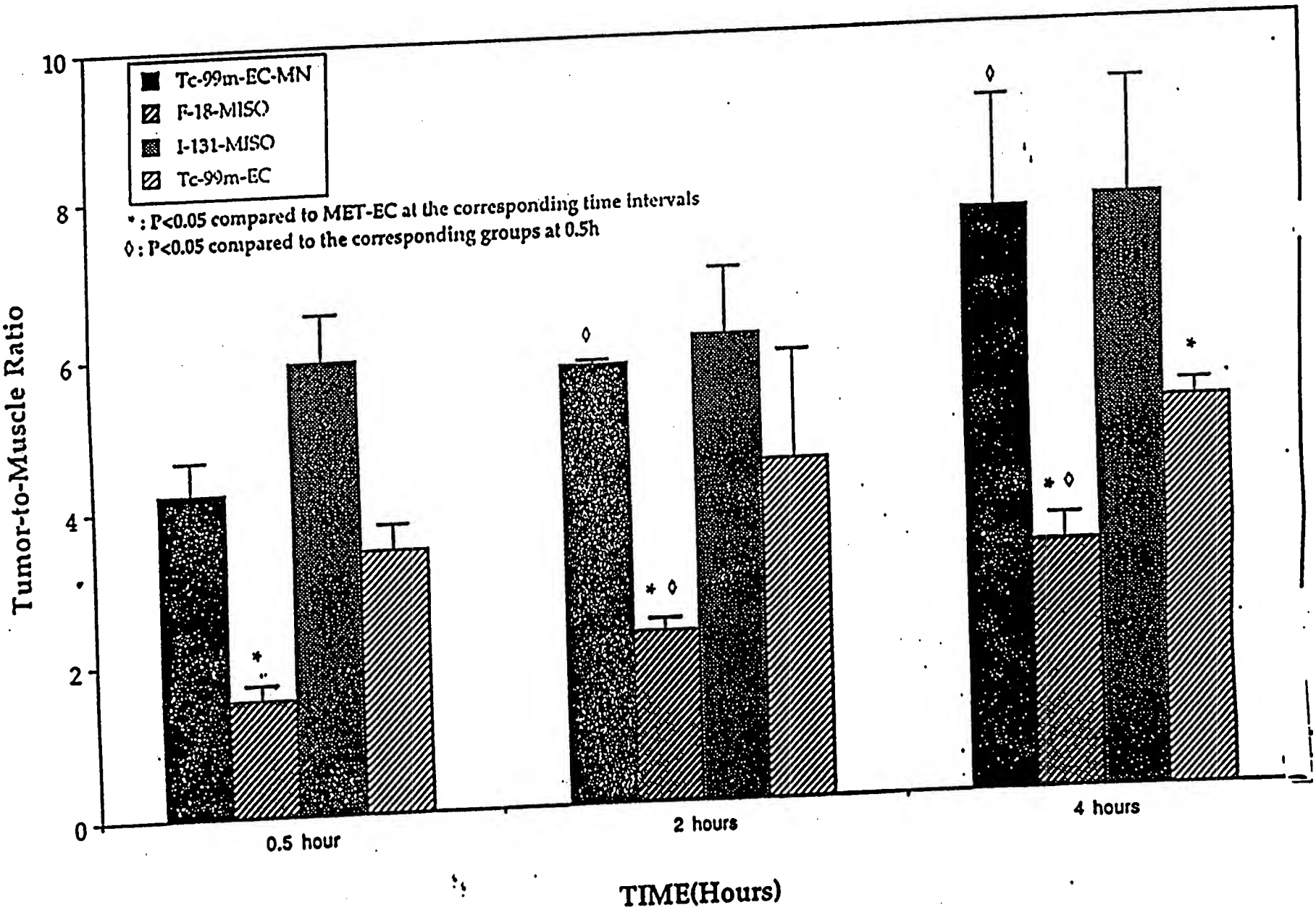

Tc-99m-EC-MN
F-18-MISO
I-131-MISO
Tc-99m-EC
* : P<0.05 compared to MET-EC at the corresponding time intervals
◊ : P<0.05 compared to the corresponding groups at 0.5h
Tumor-to-Muscle Ratio
10
8
6
4
2
0
0.5 hour
2 hours
4 hours
TIME(Hours)

FIG. 10

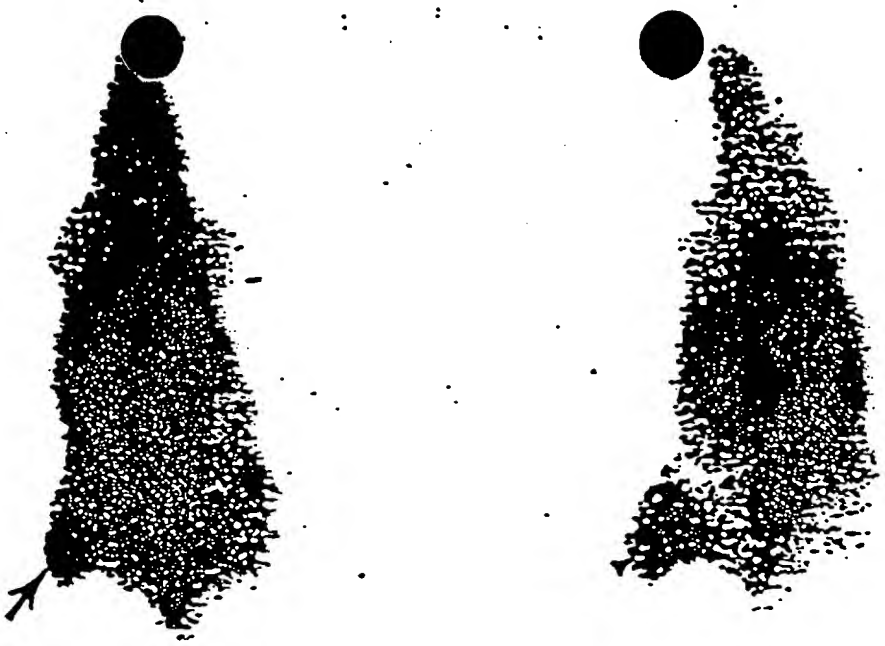


FIG. 11A

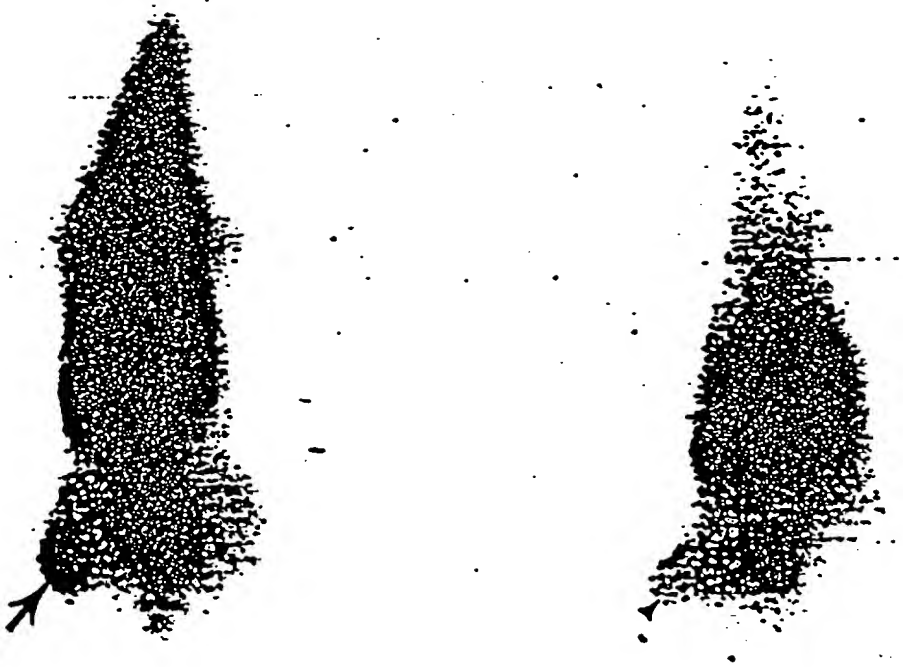


FIG. 11B

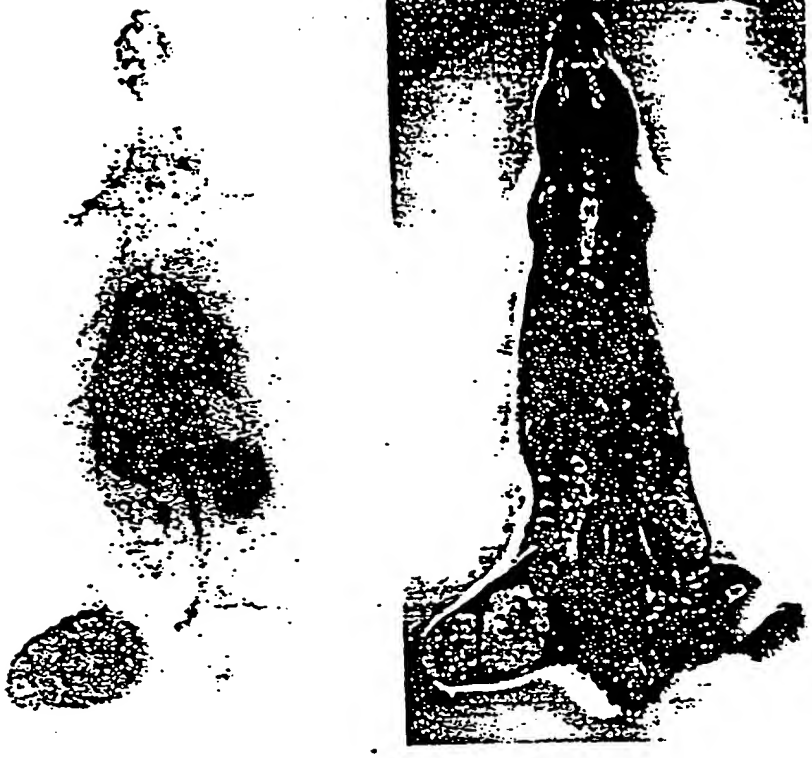


FIG. 12

3-10-1999 EC-(2-[illegible])2 after adding serum 3:

Date: Mar 10 1999 Start time: 16:02 Accum time: 00:00:50
Data File: Plate: 1 Lane: 1

Elect Resolution: NORMAL (Amp. Range: 0 - 2047)
Stop counts: 50000
Stop Counts Region: 0.00 to 20.00 cm
Rf Calculations: Origin: 1.50 cm Solvent Front: 19.00 cm
Integration Parameters: Auto Integration
Peak slope: 1.0 Min width: 0.1 Min %: 2.0

Total Count Region: 0.00cm to 20.00cm
Total Counts: 53170
Total CPM: 63810

Reg. #	Start (cm)	Stop (cm)	Center (cm)	Rf	Region Counts	Region CPM	% of Tot Reg	% of Tot Cnt
1	0.60	4.40	2.50	0.06	4557	5468	9.02	8.57
2	8.20	16.80	12.56	0.63	45980	55180	90.98	86.48
TOTAL					50540	60650	100.00	95.05

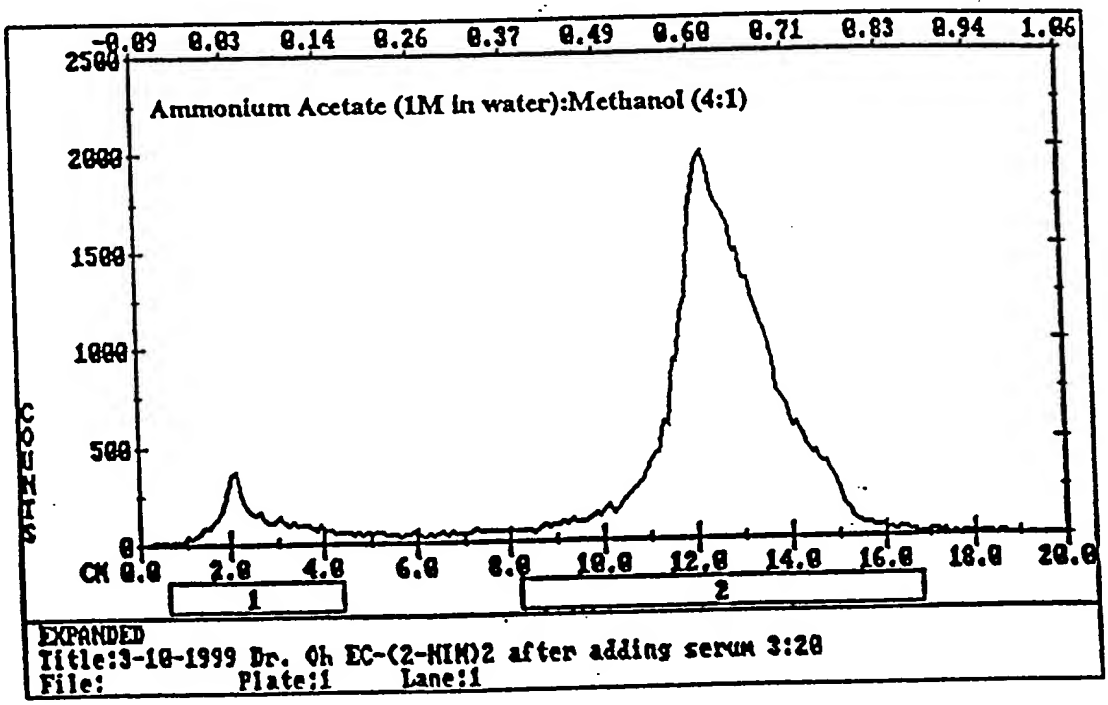


FIG. 13

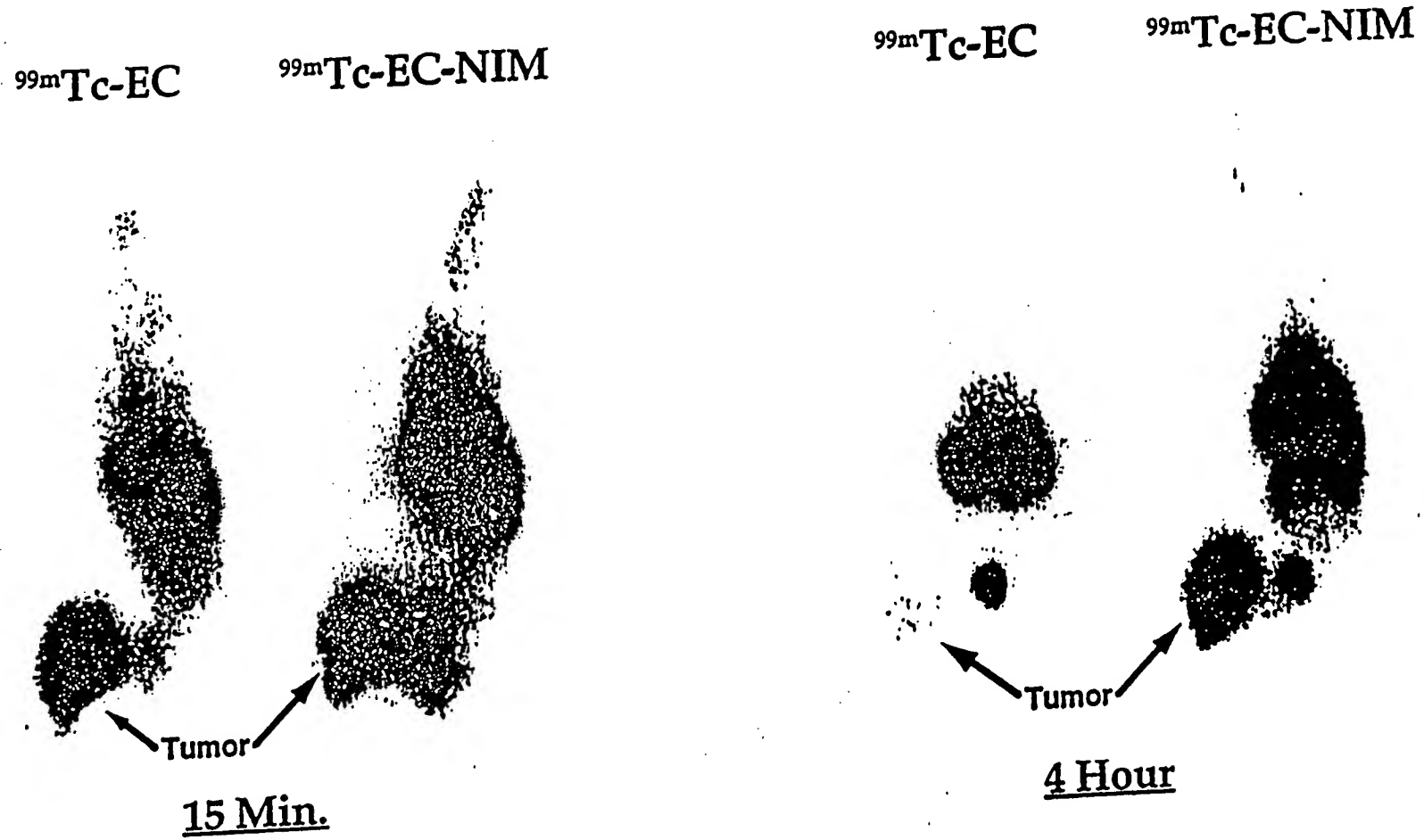


FIG. 14A

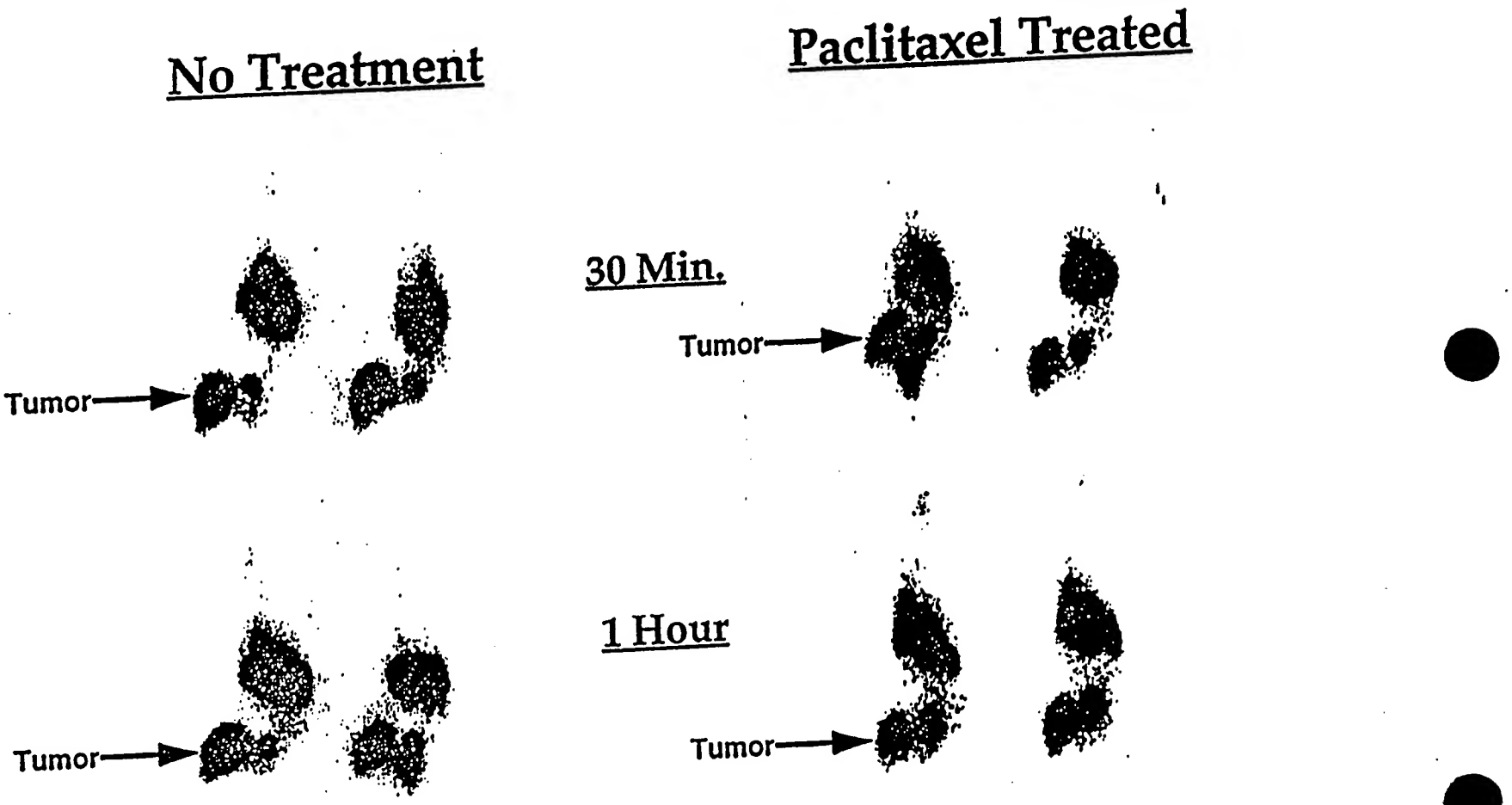


FIG. 14B

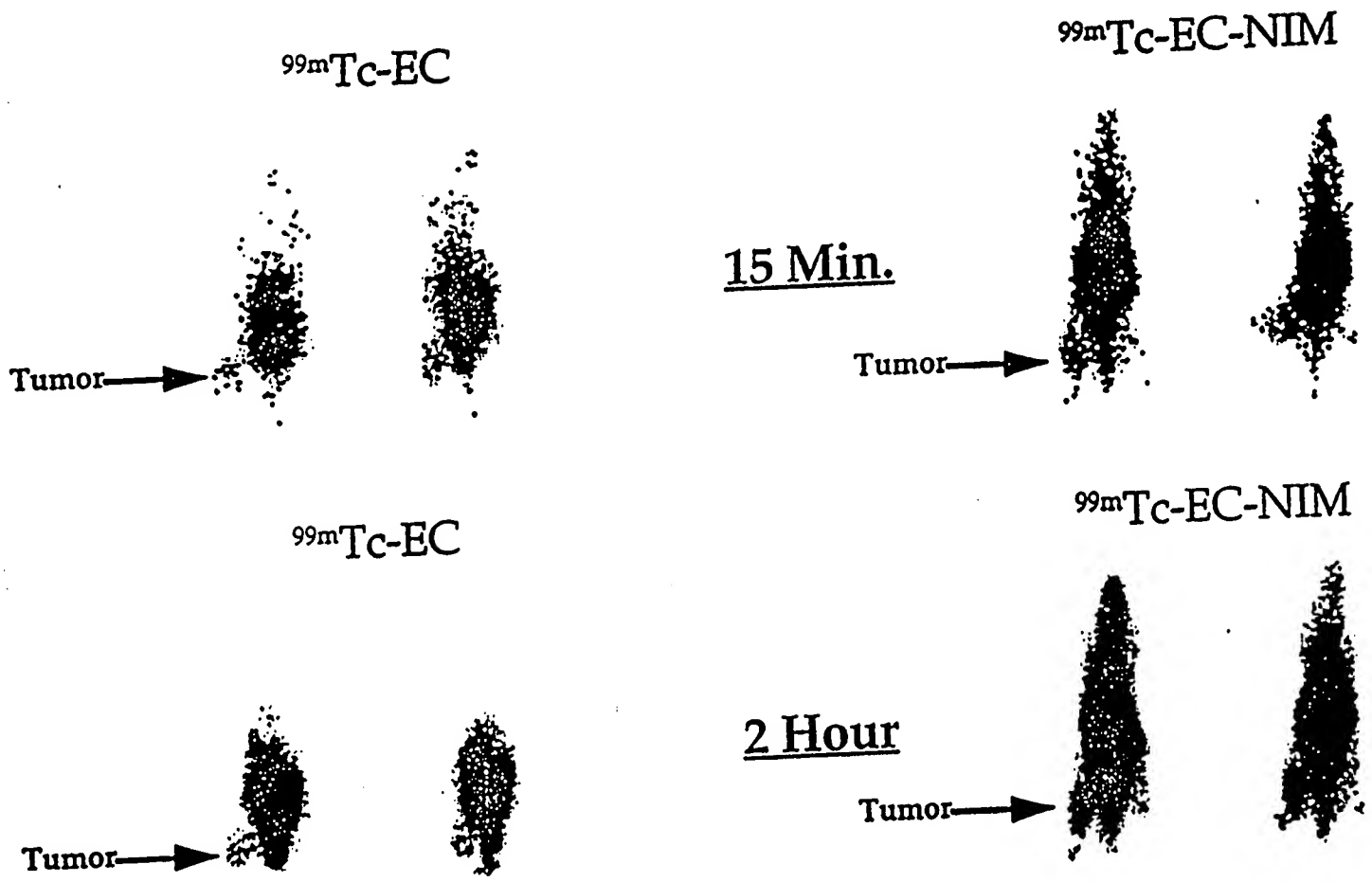


FIG. 15A

^{99m}Tc-EC-Nitroimidazole (NIM)
(100μCi/mouse, iv.)

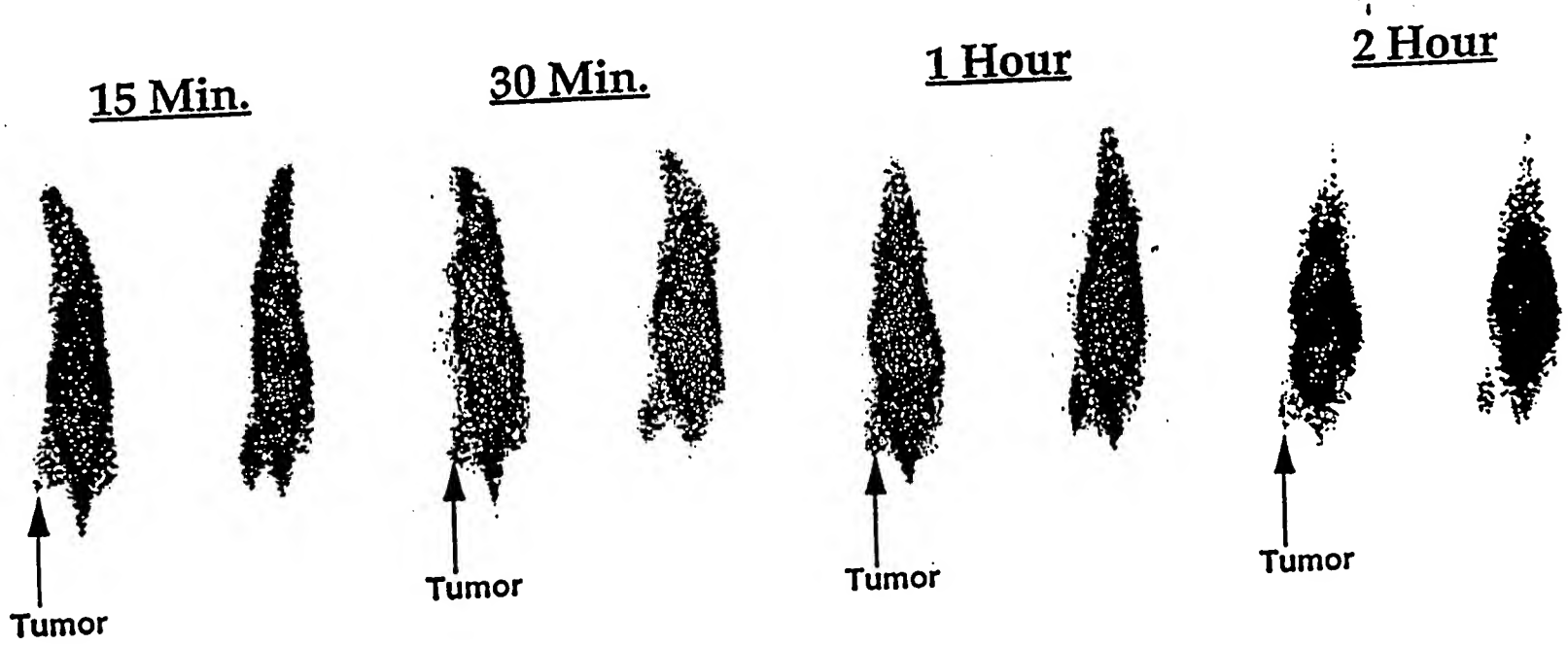


FIG. 15B

^{99m}Tc-EC-Nitroimidazole (NIM)

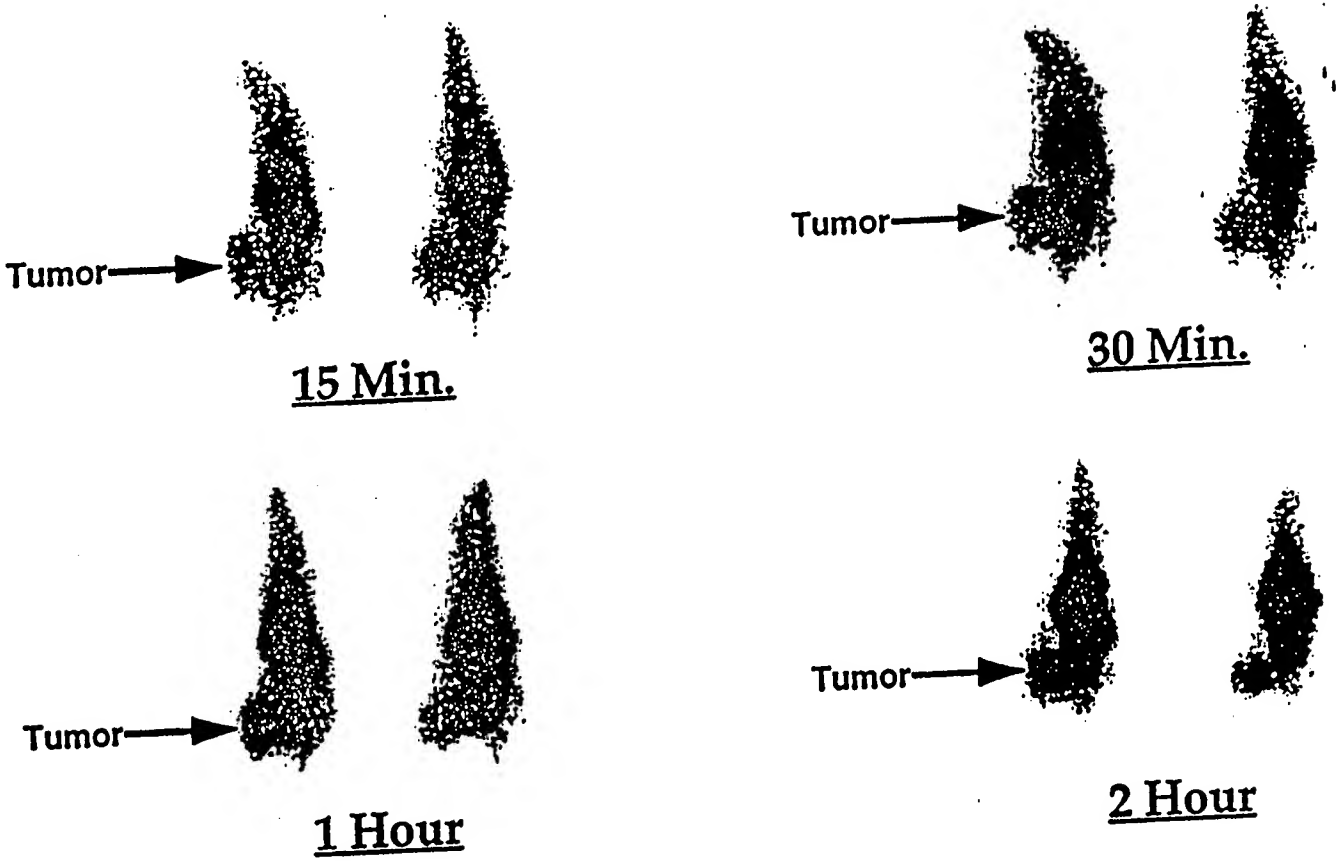


FIG. 15C

^{99m}Tc-EC-Nitroimidazole (NIM)
(100μCi/mouse, iv.)

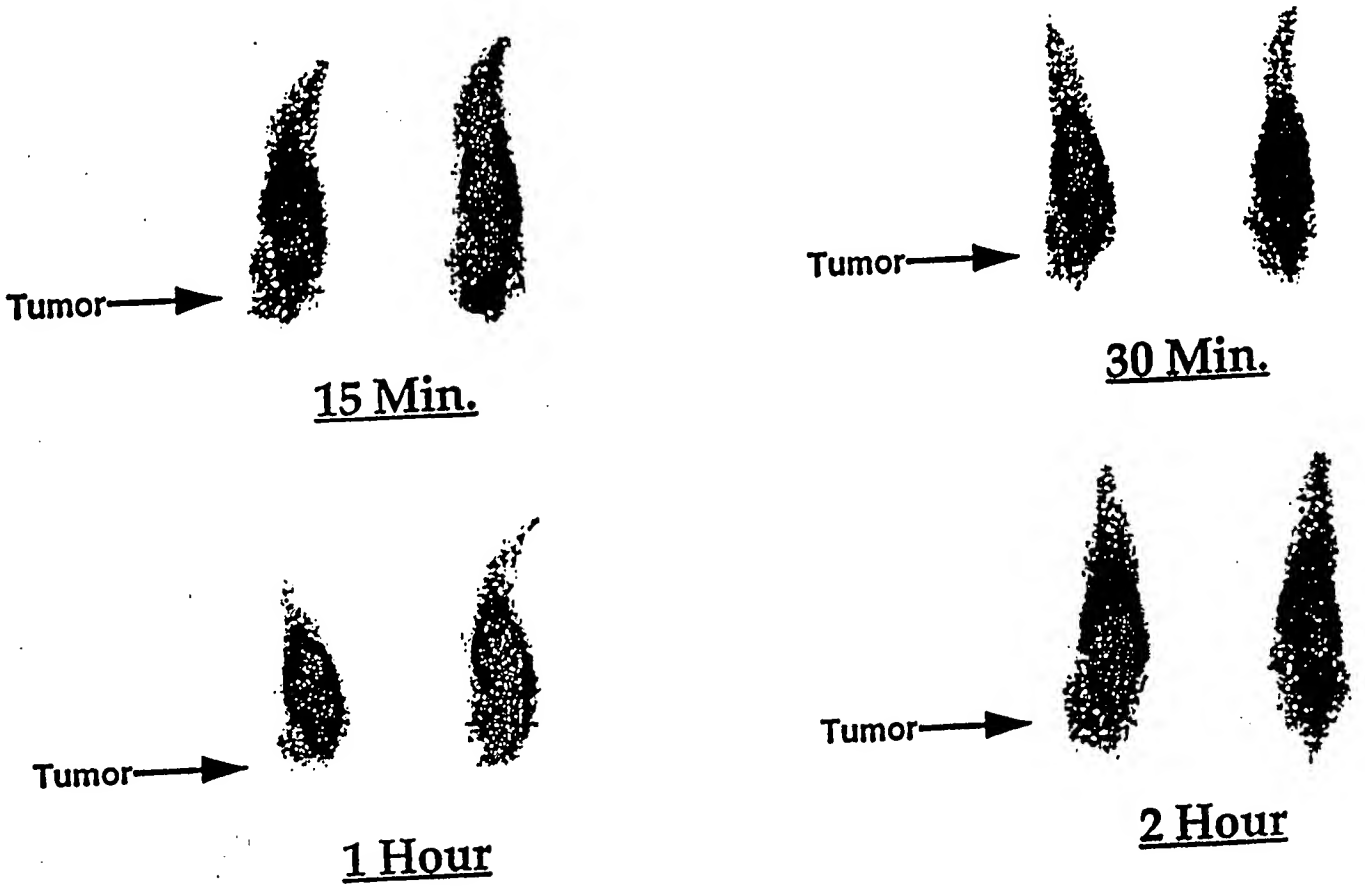
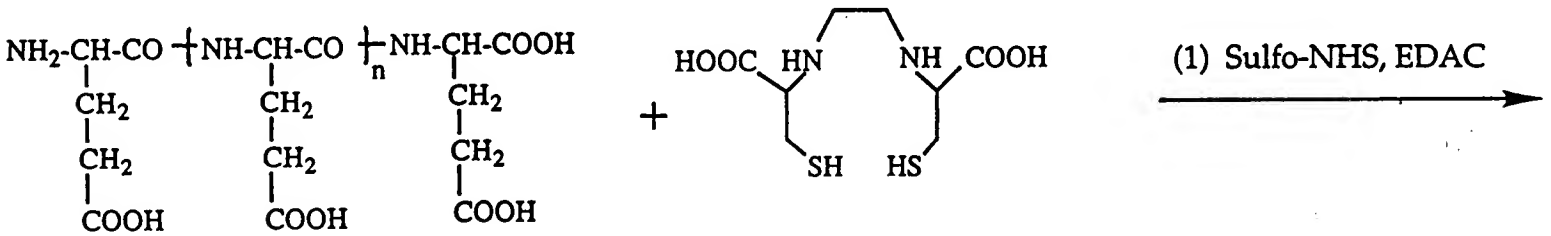
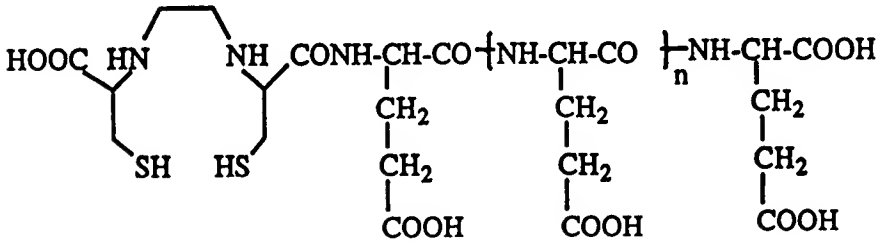


FIG. 15D



L-GAP

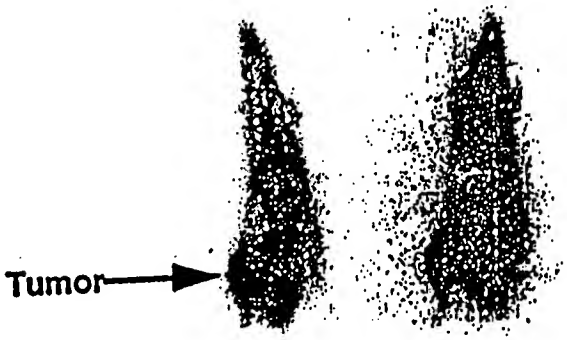
EC



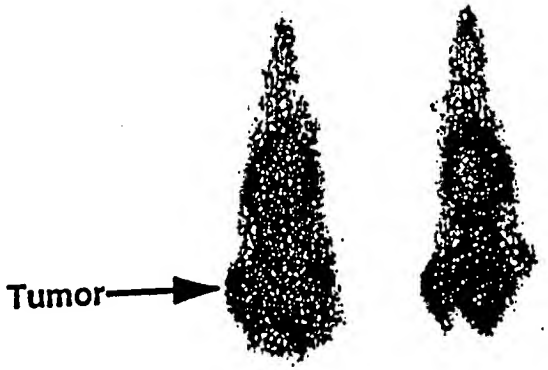
EC-GAP

Synthesis of EC-GAP

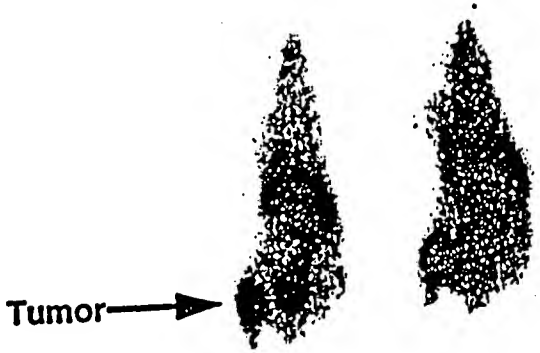
FIG. 16



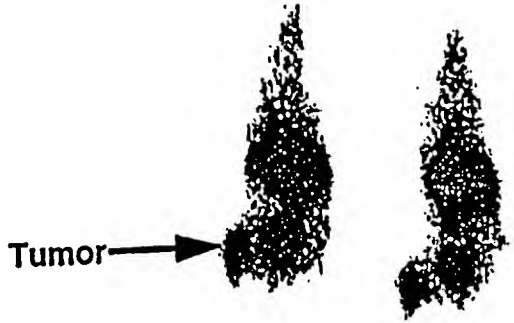
15 Min.



30 Min.



1 Hour



2 Hour

FIG. 17

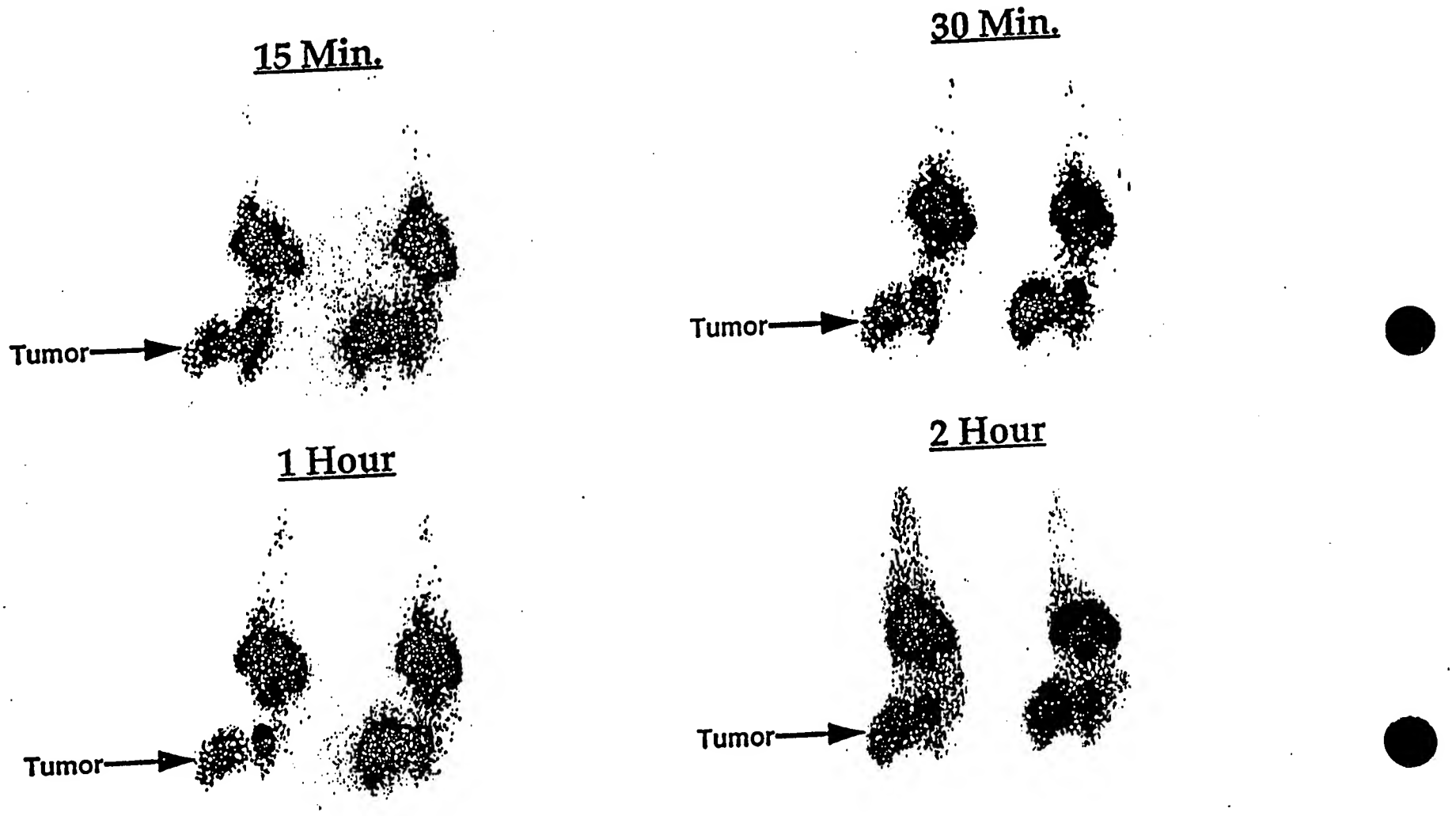


FIG. 18

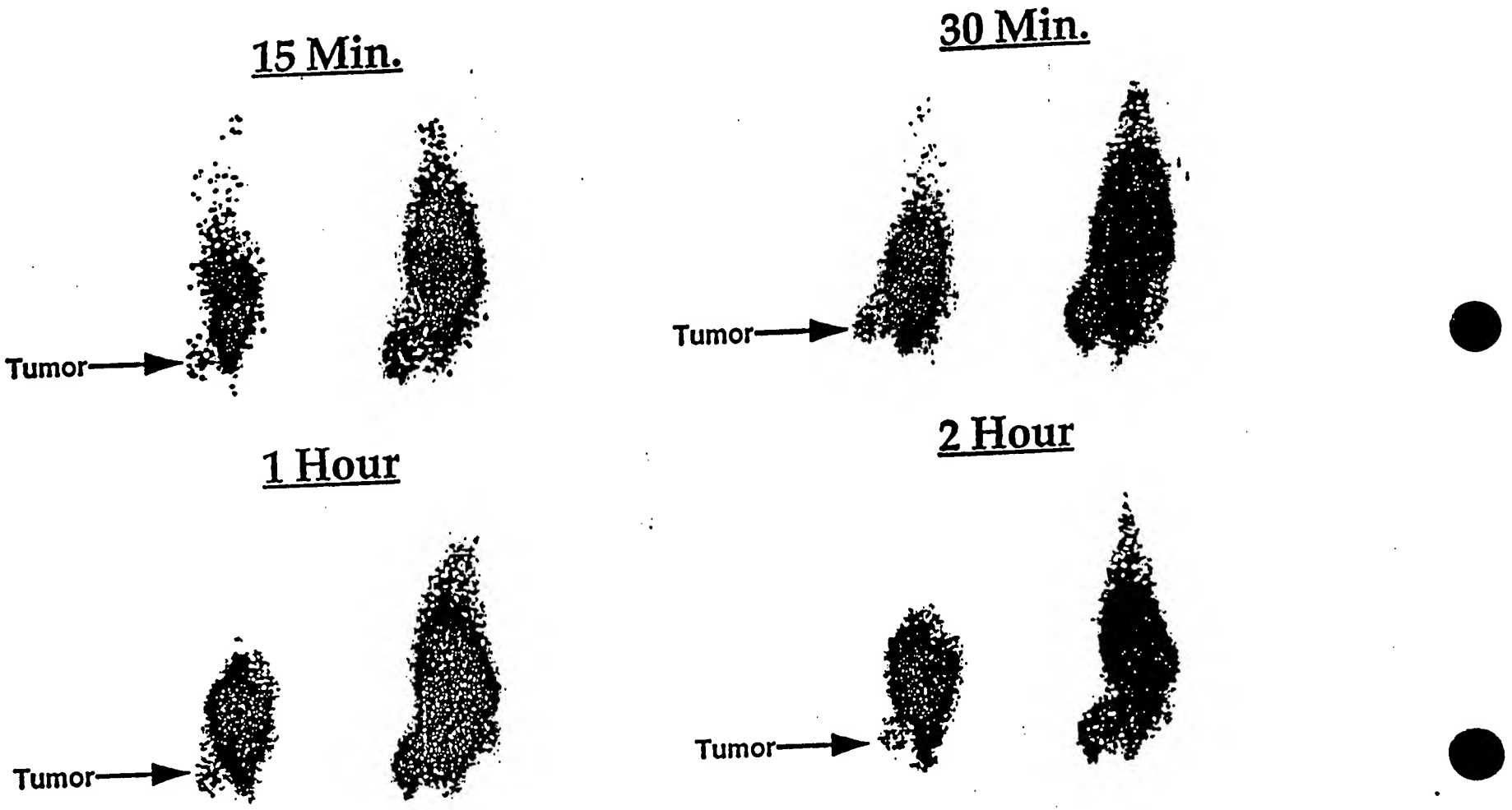


FIG. 19A

^{99m}Tc-EC-Annexin V
(100μCi/mouse, iv.)

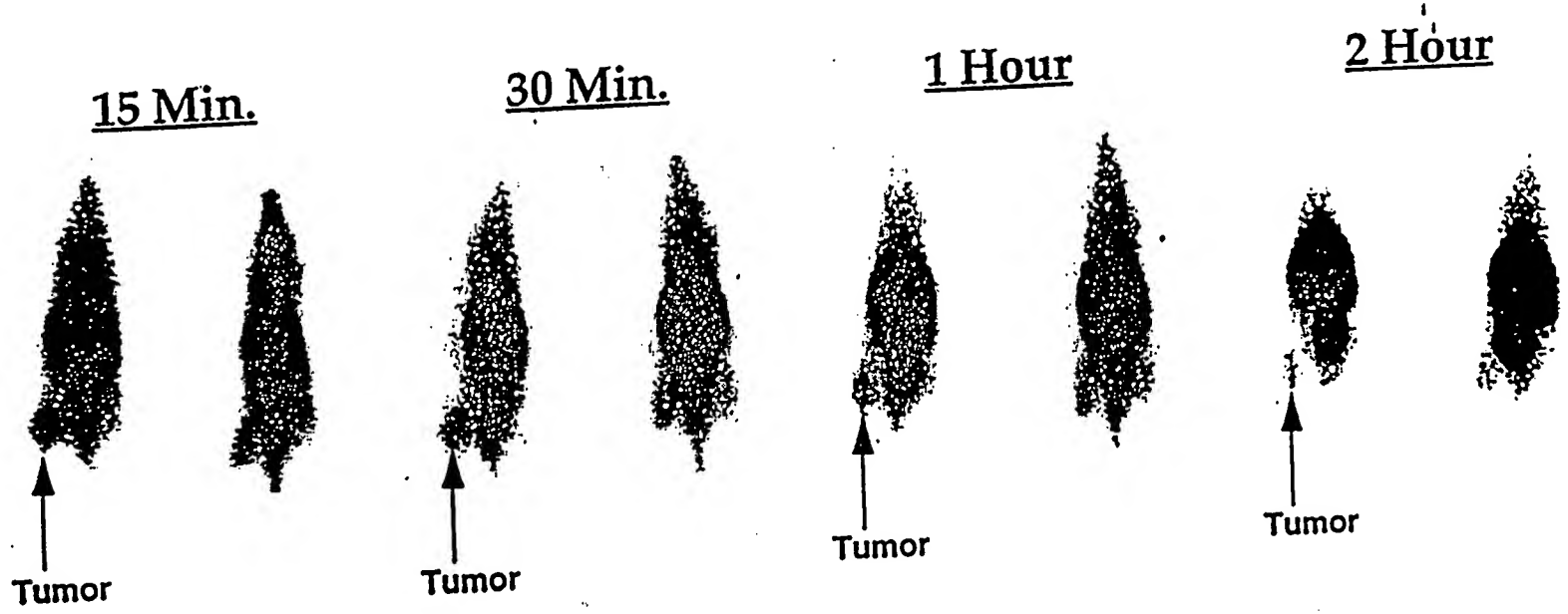


FIG. 19B

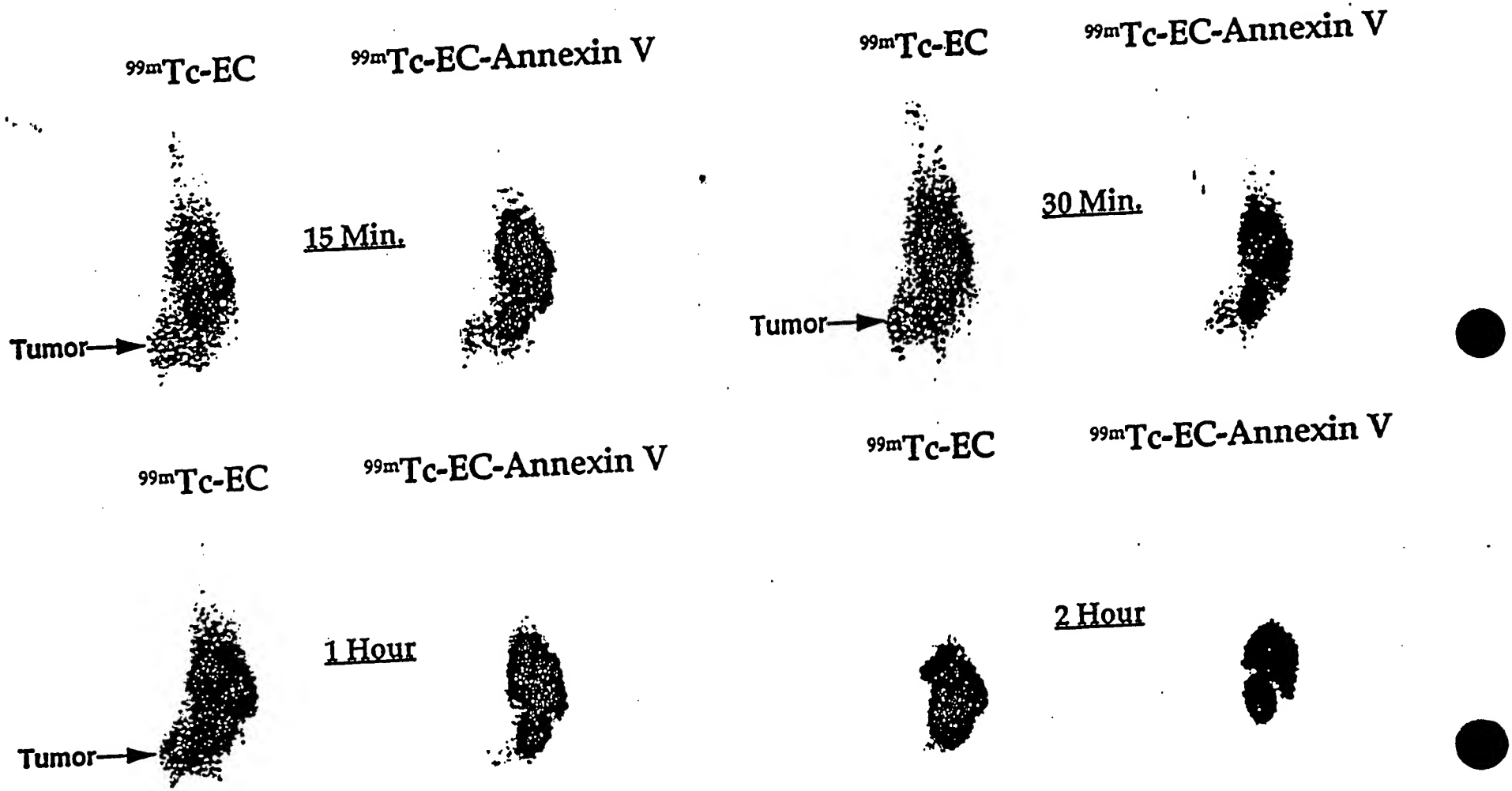
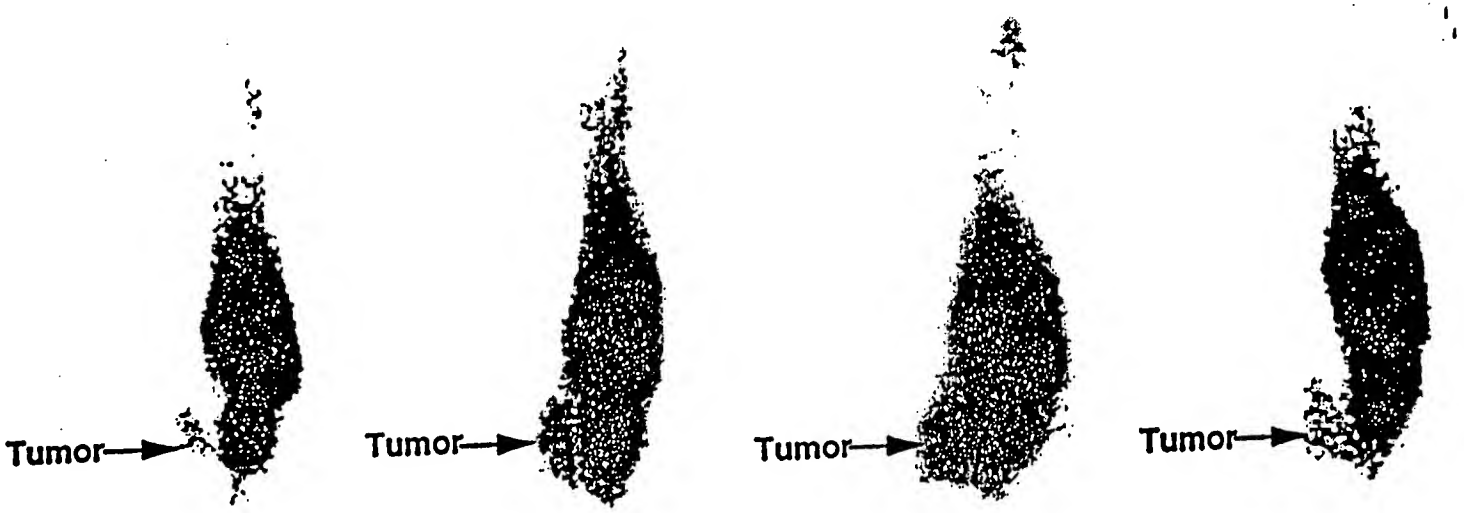


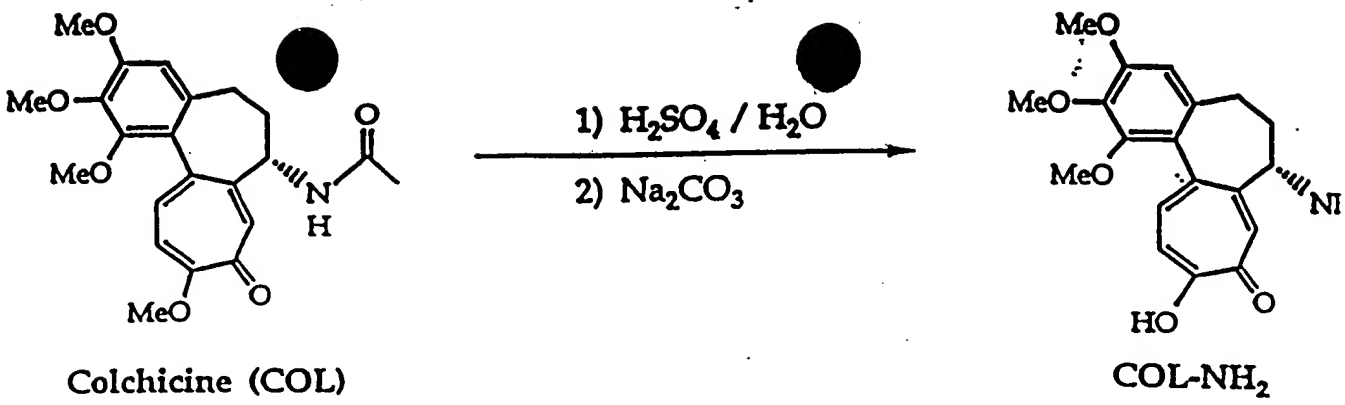
FIG. 20A

^{99m}Tc-EC-Annexin V
(100μCi/mouse, iv.)



15 Min. 30 Min. 1 Hour 2 Hour

FIG. 20B

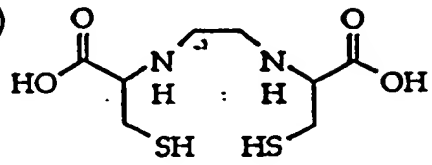


Colchicine (COL)

COL-NH_2

1) COL-NH_2

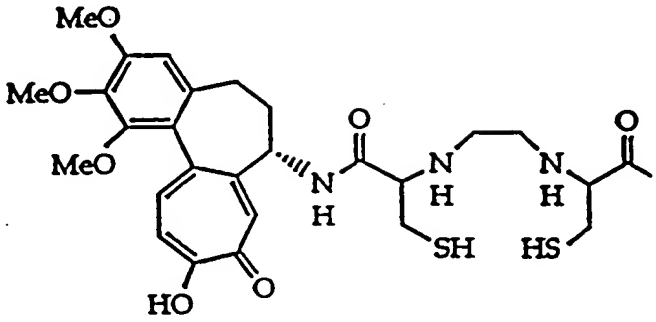
2)



EC

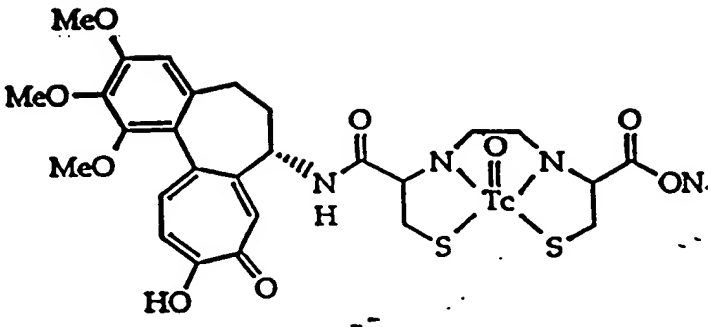
3) 1N-NaOH

4) EDC-HCl / Sulfo-NHS



EC-COL

$Na^{99m}TcO_4$ / $SnCl_2$



^{99m}Tc-EC-COL

FIG. 21

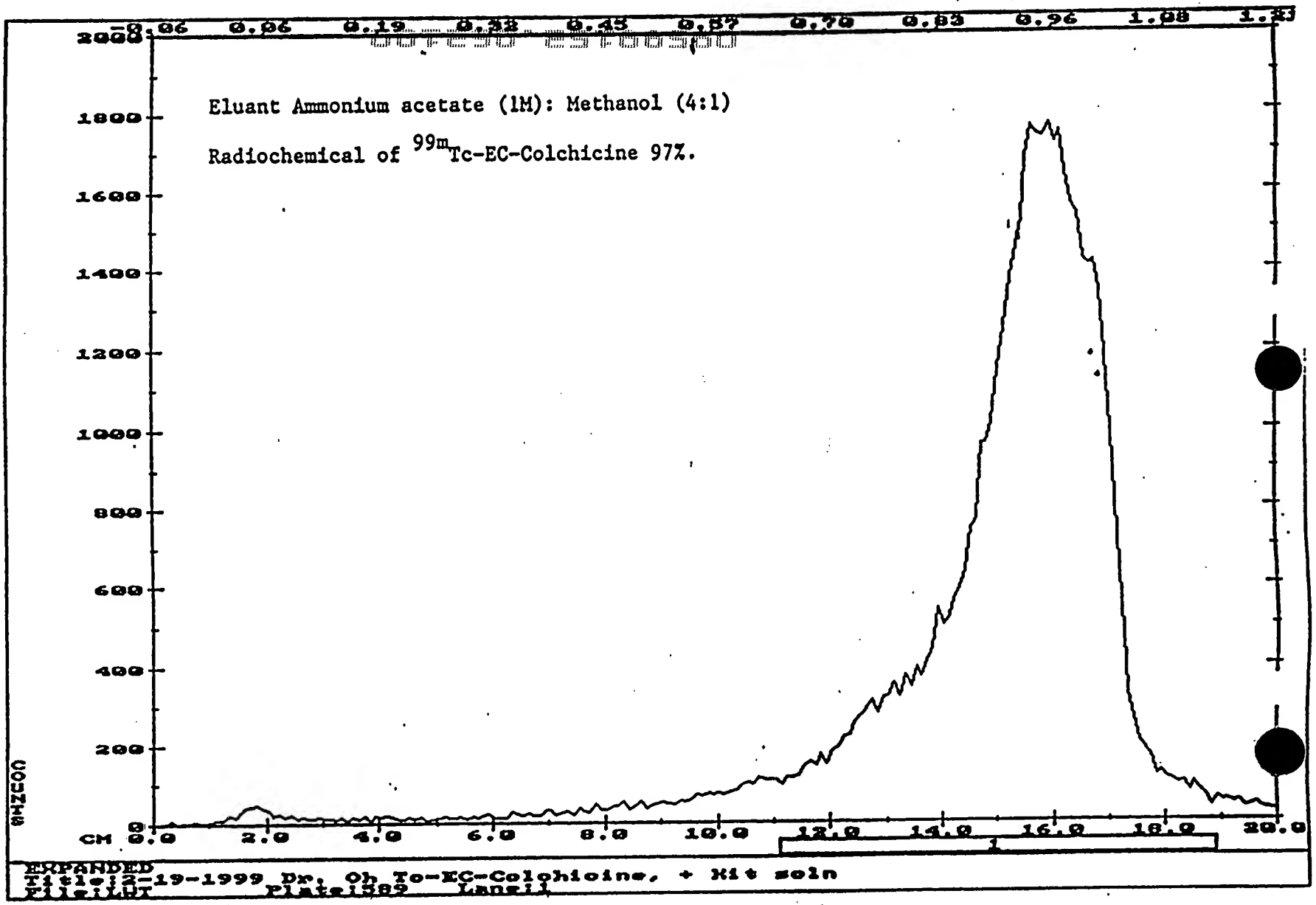

Eluant Ammonium acetate (1M): Methanol (4:1)
Radiochemical of 99mTc-EC-Colchicine 97%.
0.06 0.06 0.19 0.32 0.45 0.57 0.70 0.83 0.96 1.08
2000
1800
1600
1400
1200
1000
800
600
400
200
0
COUNTS
CM 0.0 2.0 4.0 6.0 8.0 10.0 12.0 14.0 16.0 18.0 20.0
EXPANDED
Title:2-19-1999 Dr. Oh Tc-EC-Colchicine, + Kit soln
File:LHT Plate1582 Lansil

FIG. 22

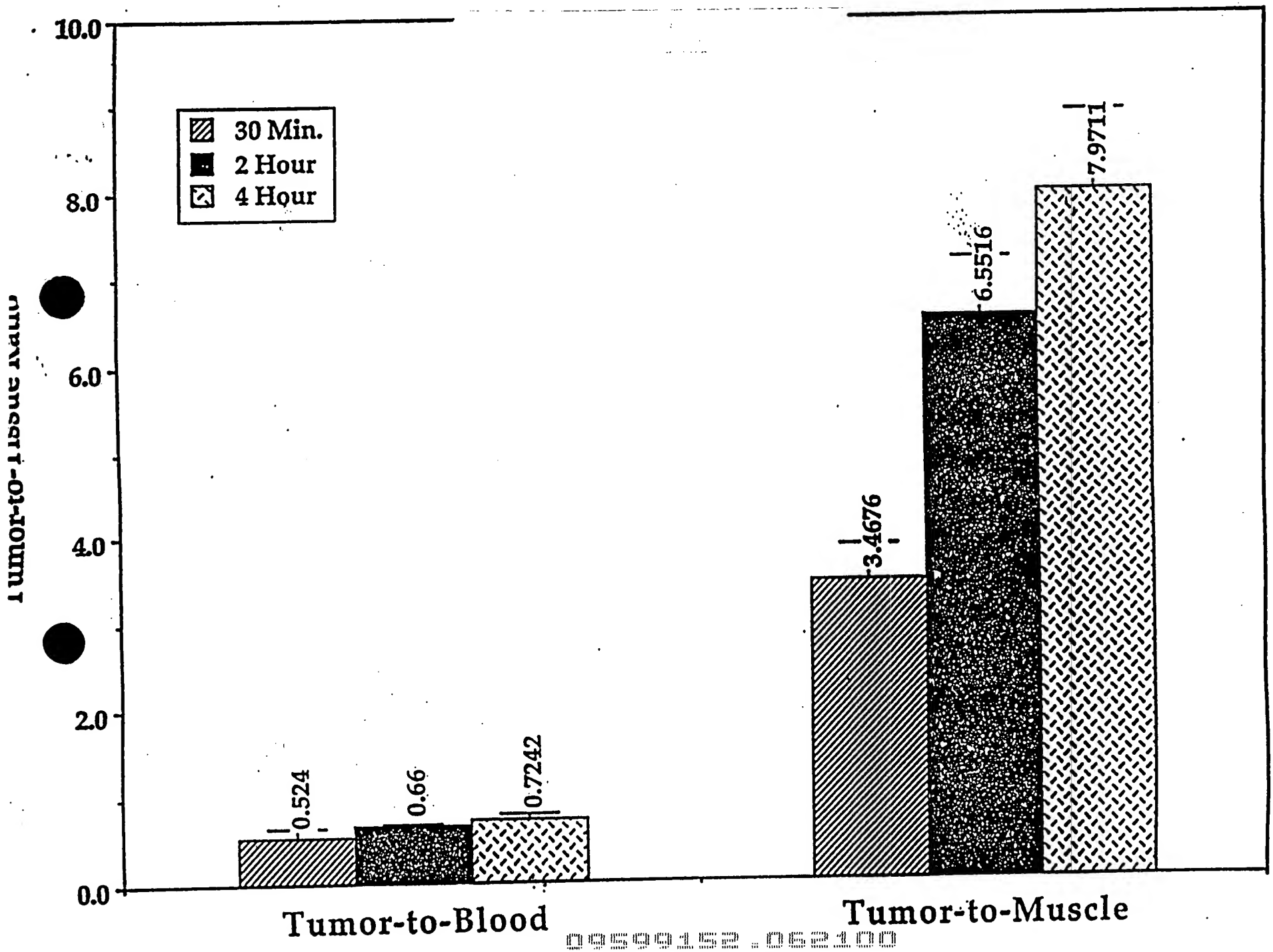


FIG. 23

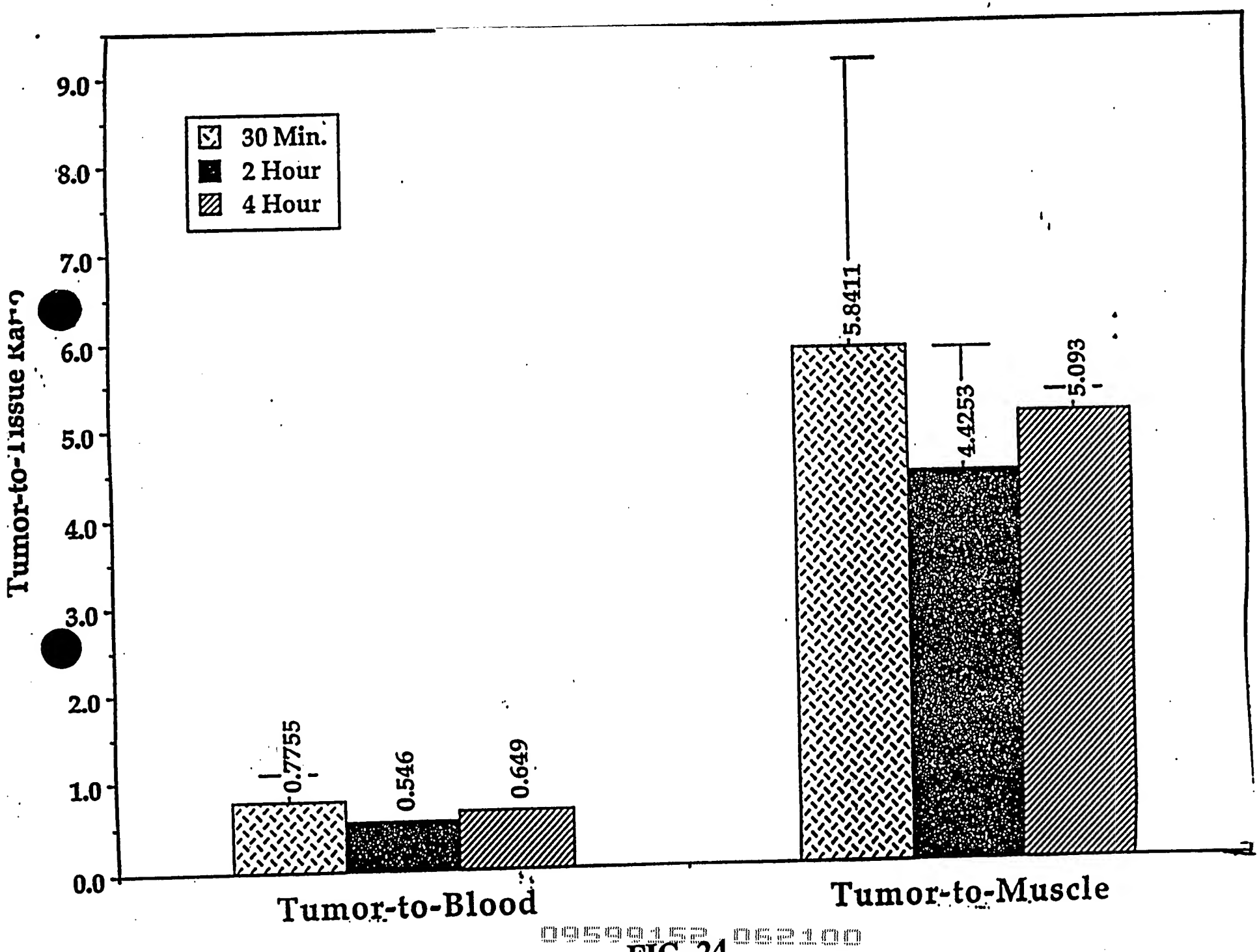

9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
30 Min.
2 Hour
4 Hour
0.7755
0.546
0.649
5.8411
4.4253
5.093
Tumor-to-Blood
Tumor-to-Muscle

FIG. 24

^{99m}Tc-EC-Colchicine (1 Hour Postinjection)

FIG. 25

^{99m}Tc-EC (Control) (1 Hour Postinjection)

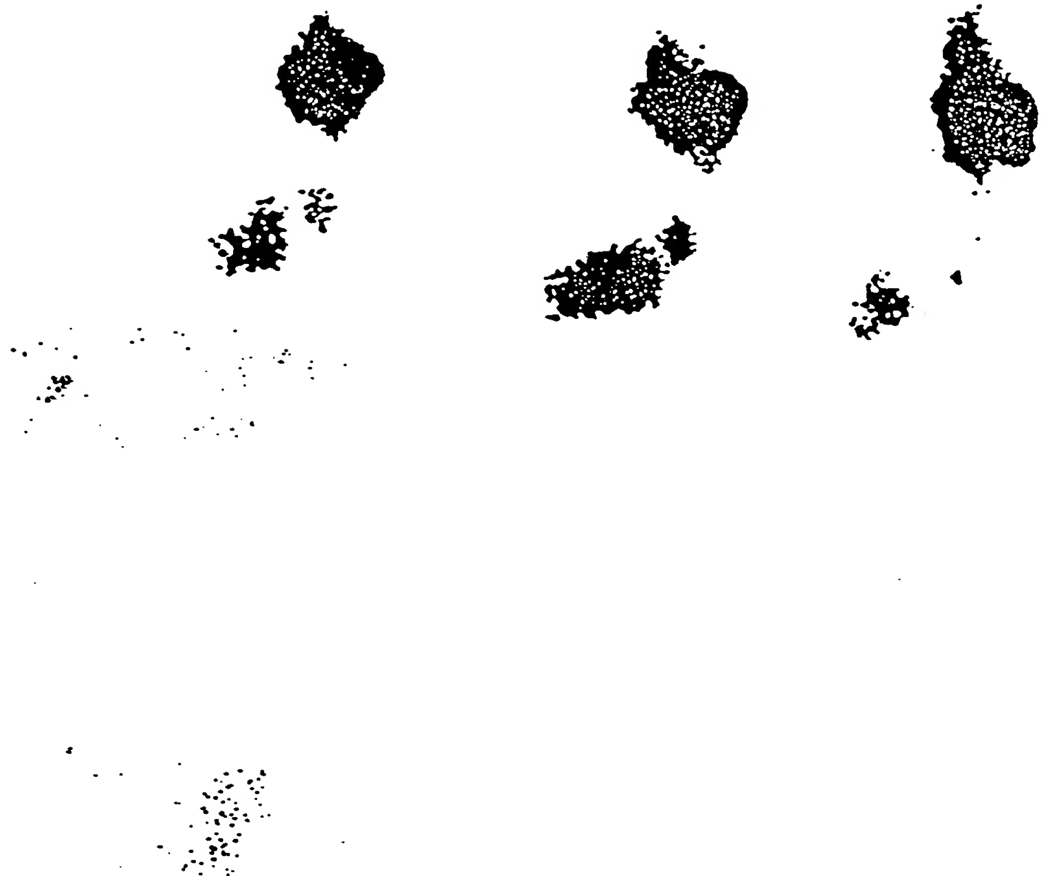


FIG. 26

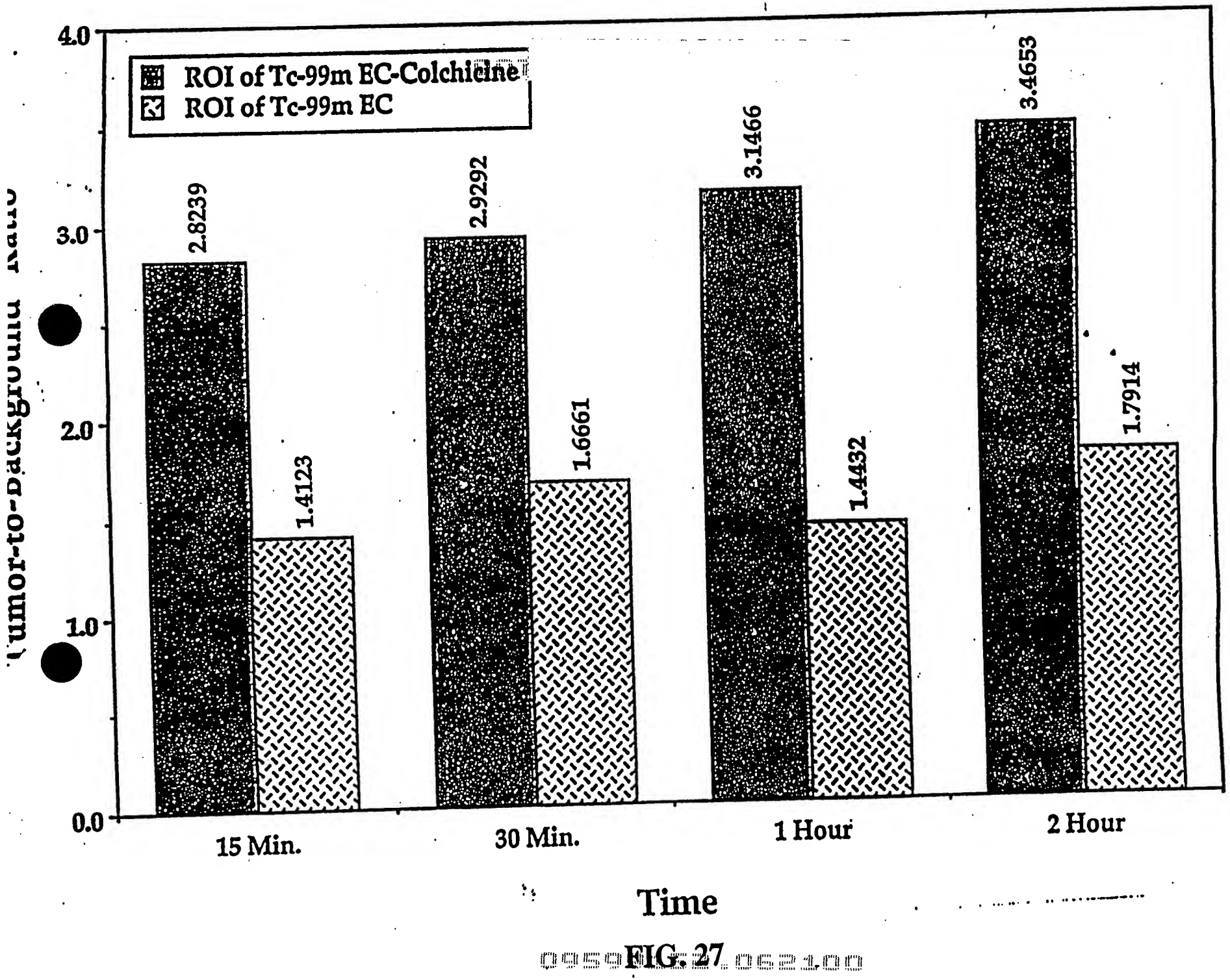

ROI of Tc-99m EC-Colchicine
ROI of Tc-99m EC
4.0
3.0
2.0
1.0
0.0
2.8239
1.4123
2.9292
1.6661
3.1466
1.4432
3.4653
1.7914
15 Min.
30 Min.
1 Hour
2 Hour
Time

FIG. 27

FIG. 28

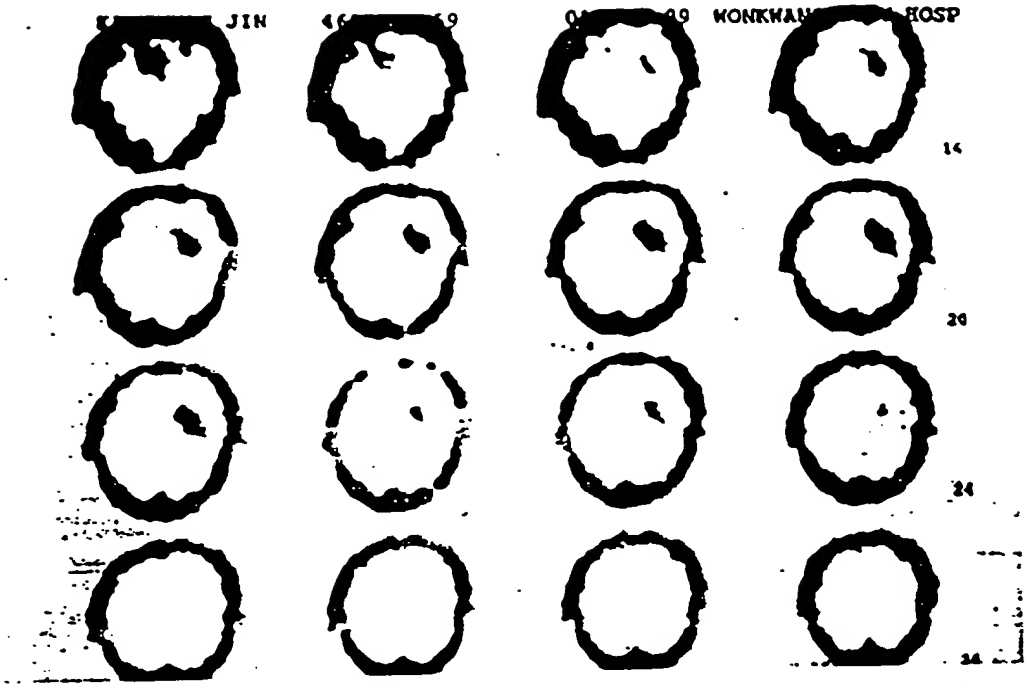


FIG. 29

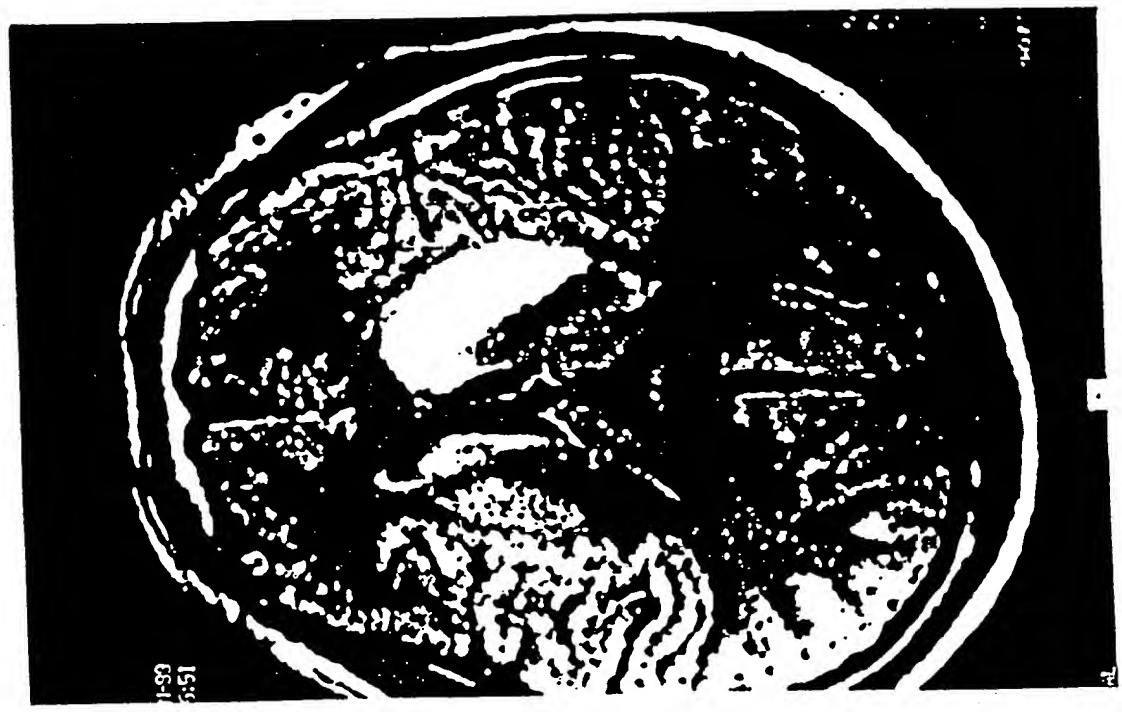


FIG. 30

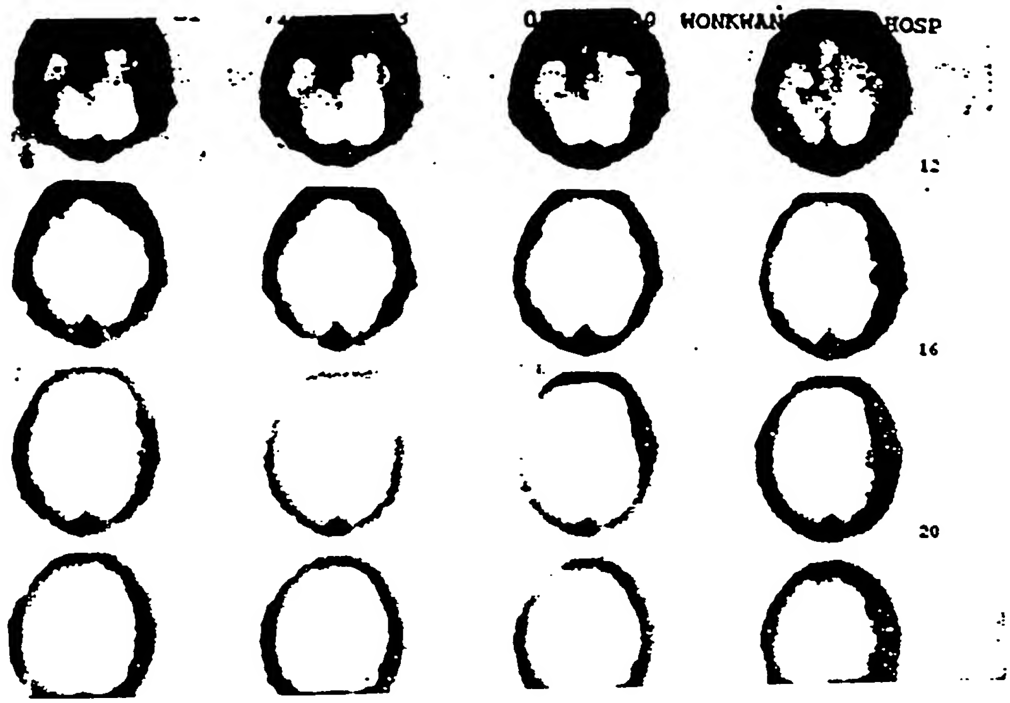


FIG. 31

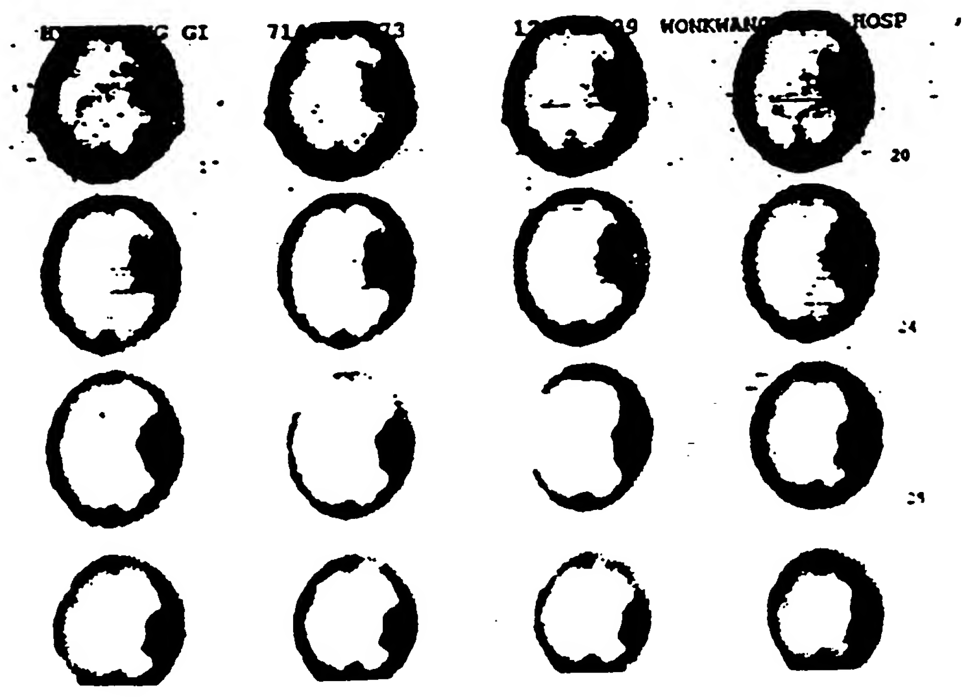


FIG. 32

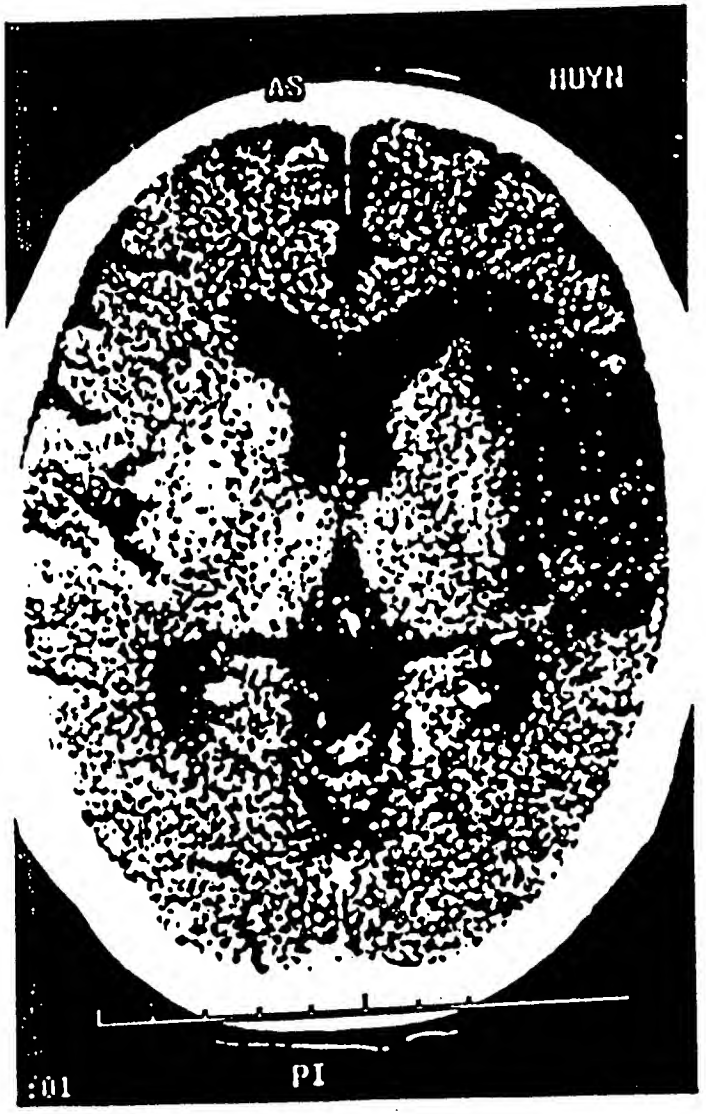


FIG. 33

FIG. 34

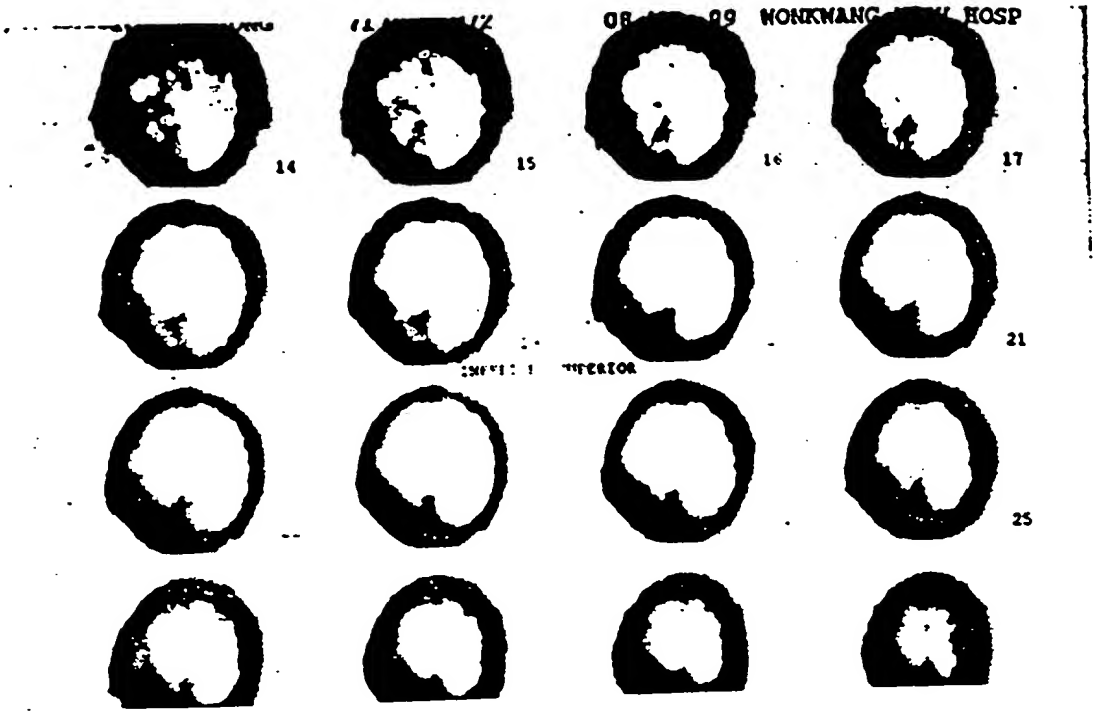
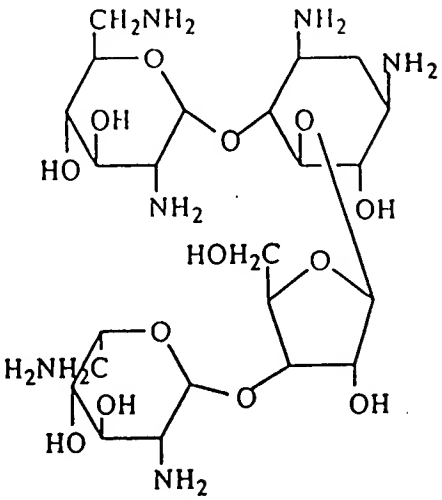
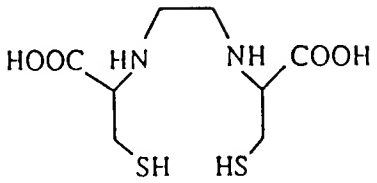


FIG. 35



Neomycin

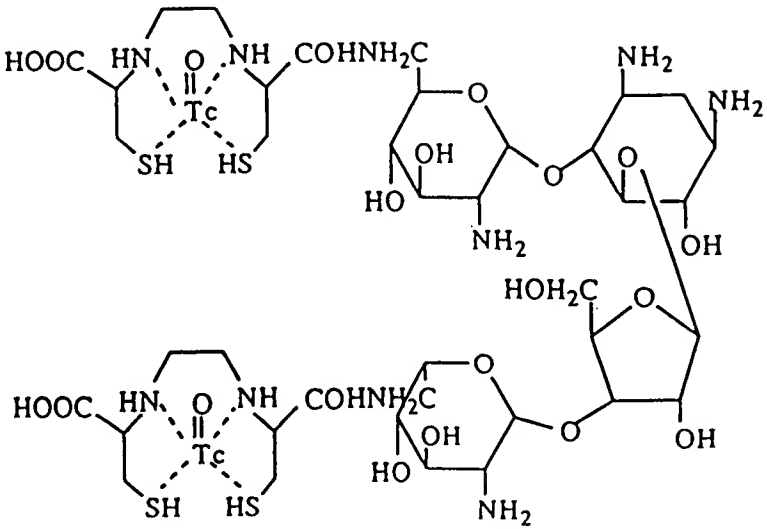
+



EC

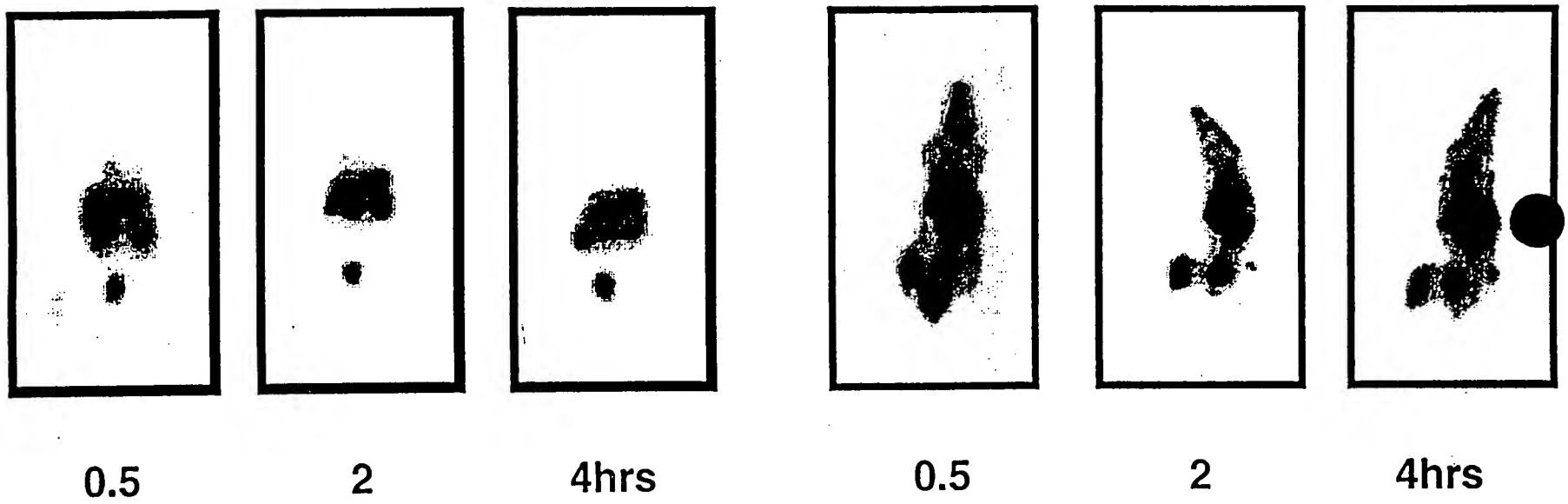
(1) Sulfo-NHS, EDAC

(2) $NaTcO_4/SnCl_2$



^{99m}Tc-EC-Neomycin

FIG. 36 Synthetic scheme of ^{99m}Tc-EC-neomycin.



Planar image of breast tumor-bearing rats after administration of ^{99m}Tc-EC and ^{99m}Tc-EC-Neomycin (100μCi/rat, iv.) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

FIG. 37A Scintigraphic image of breast tumor-bearing rats after administration of ^{99m}Tc-EC and ^{99m}Tc-EC-neomycin (100 μCi/rat, iv.) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

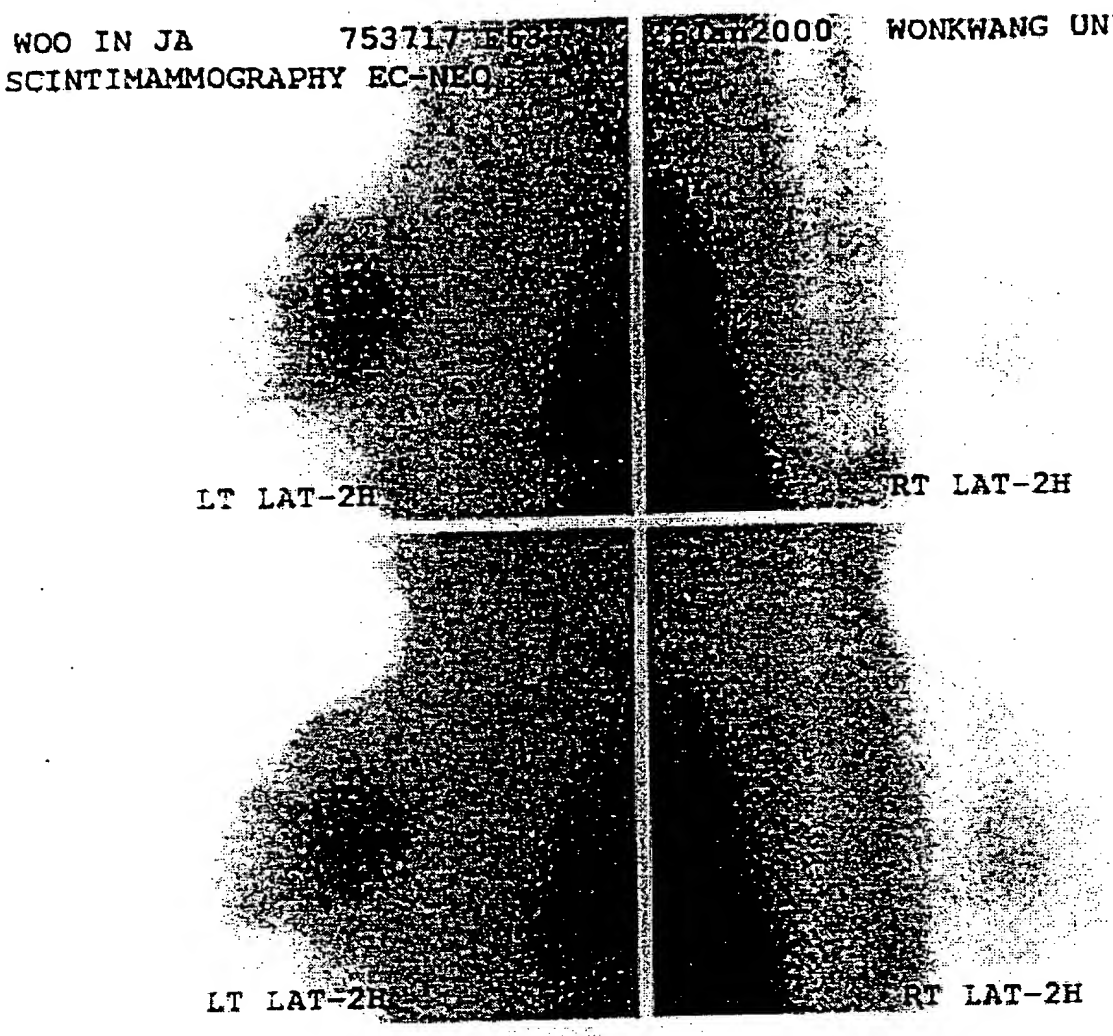
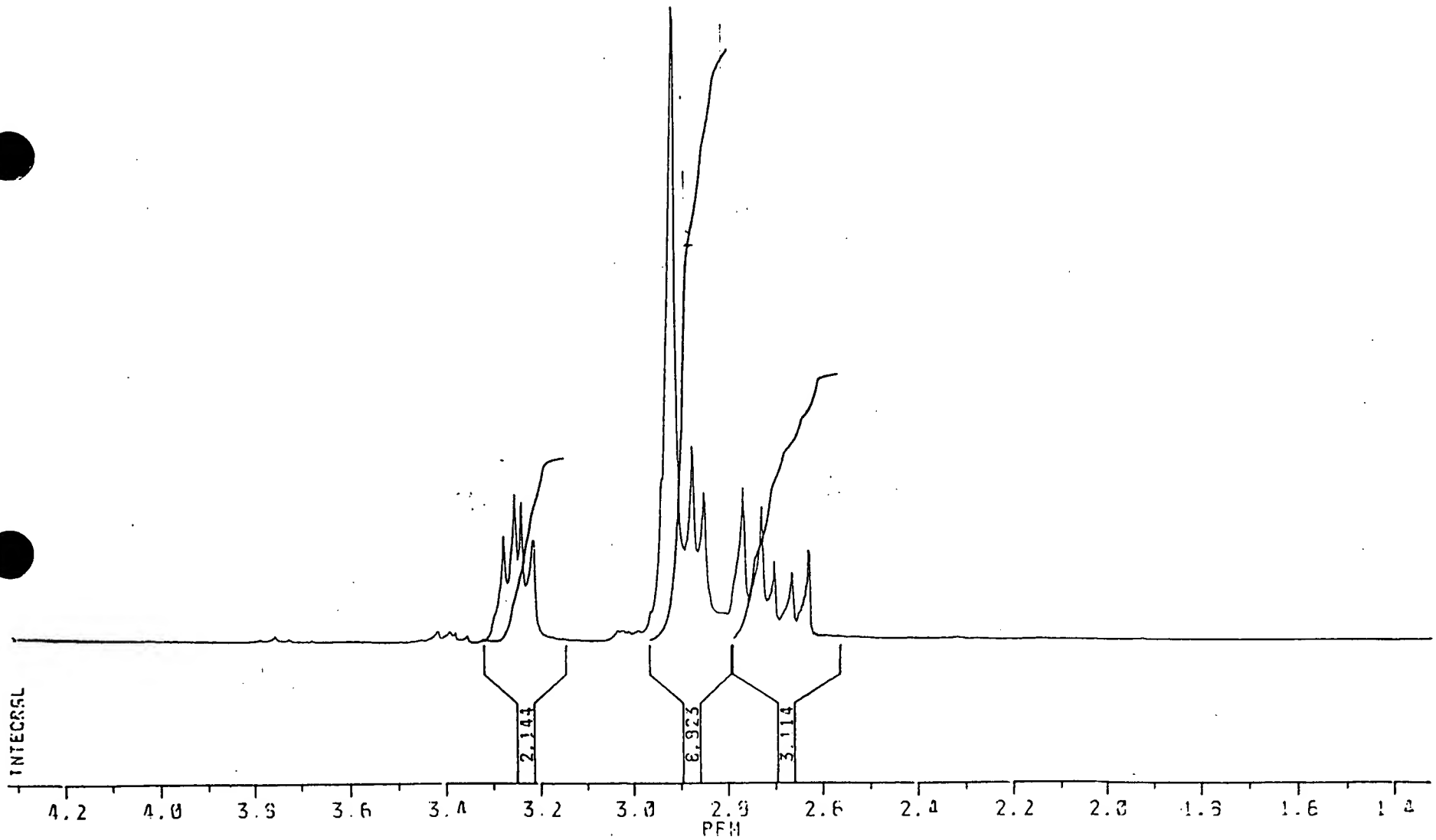


FIG. 37B Scintimammography with ^{99m}Tc-EC- neomycin (30 mCi, iv.) of a breast cancer patient. Images taken two hours post-injection.

EC



^{1}H NMR of EC

FIG. 38A

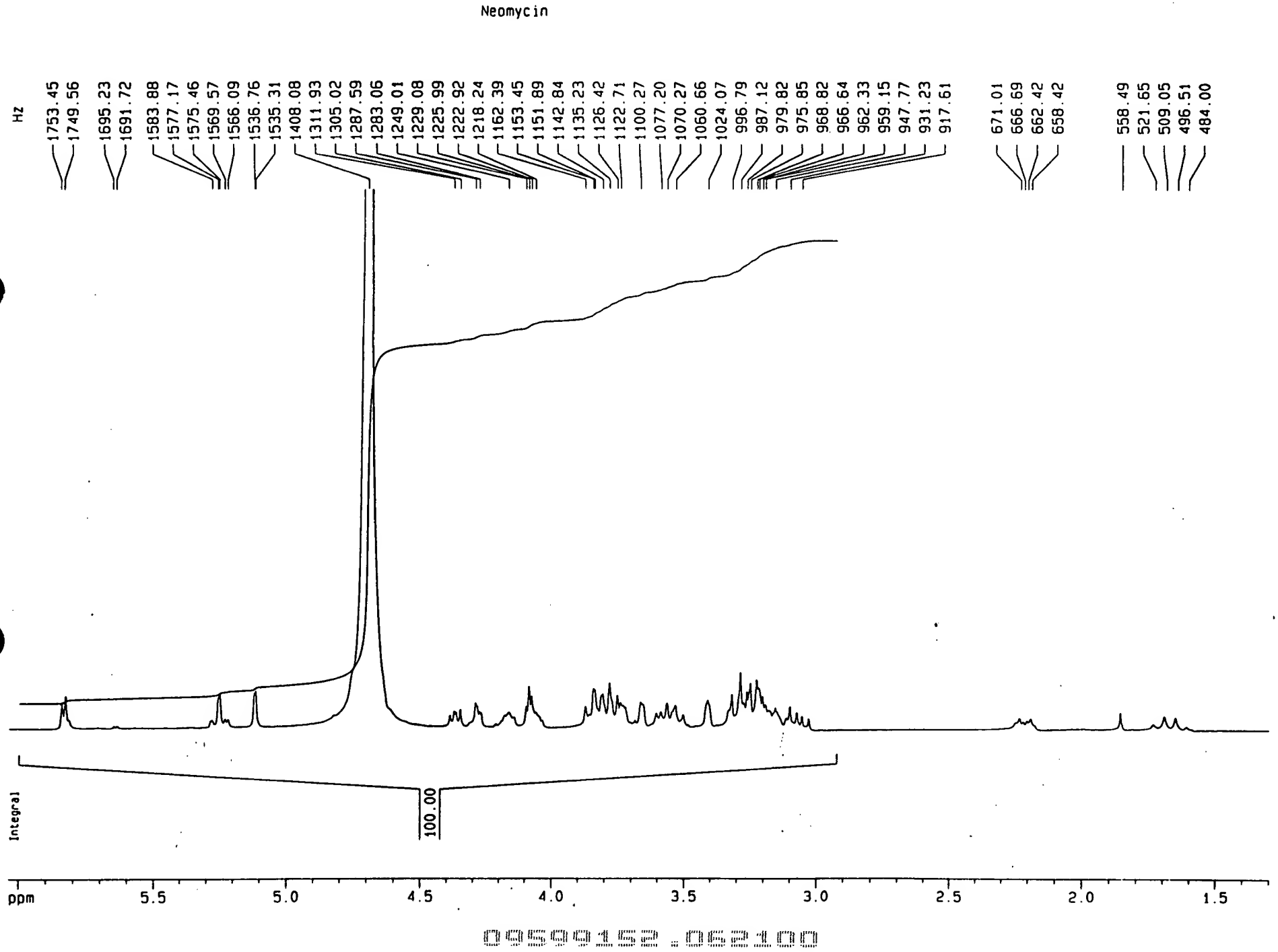
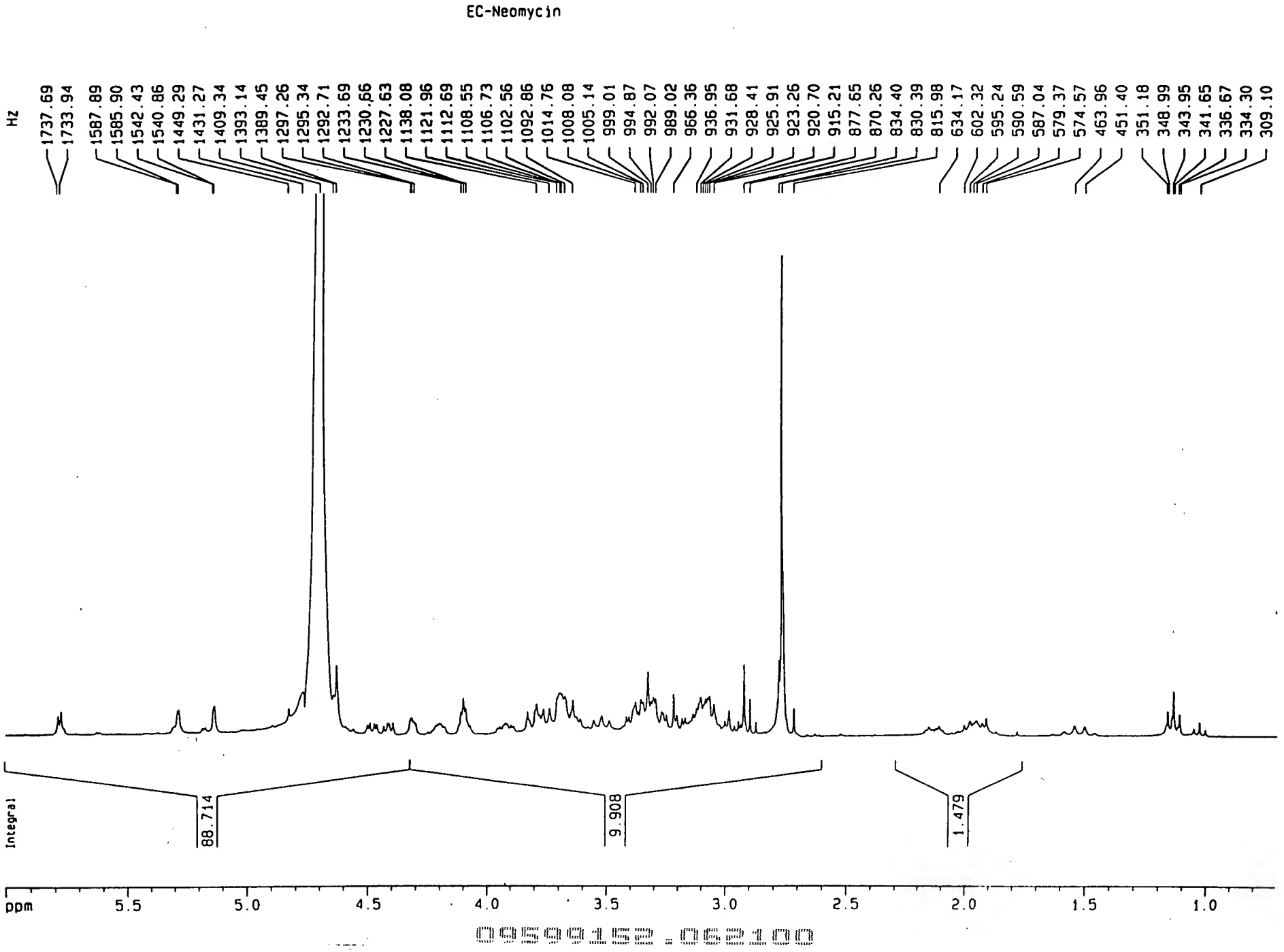


FIG. 38B ^{1}H-NMR of neomycin.



^{1}H-NMR of EC-neomycin.

FIG. 38C

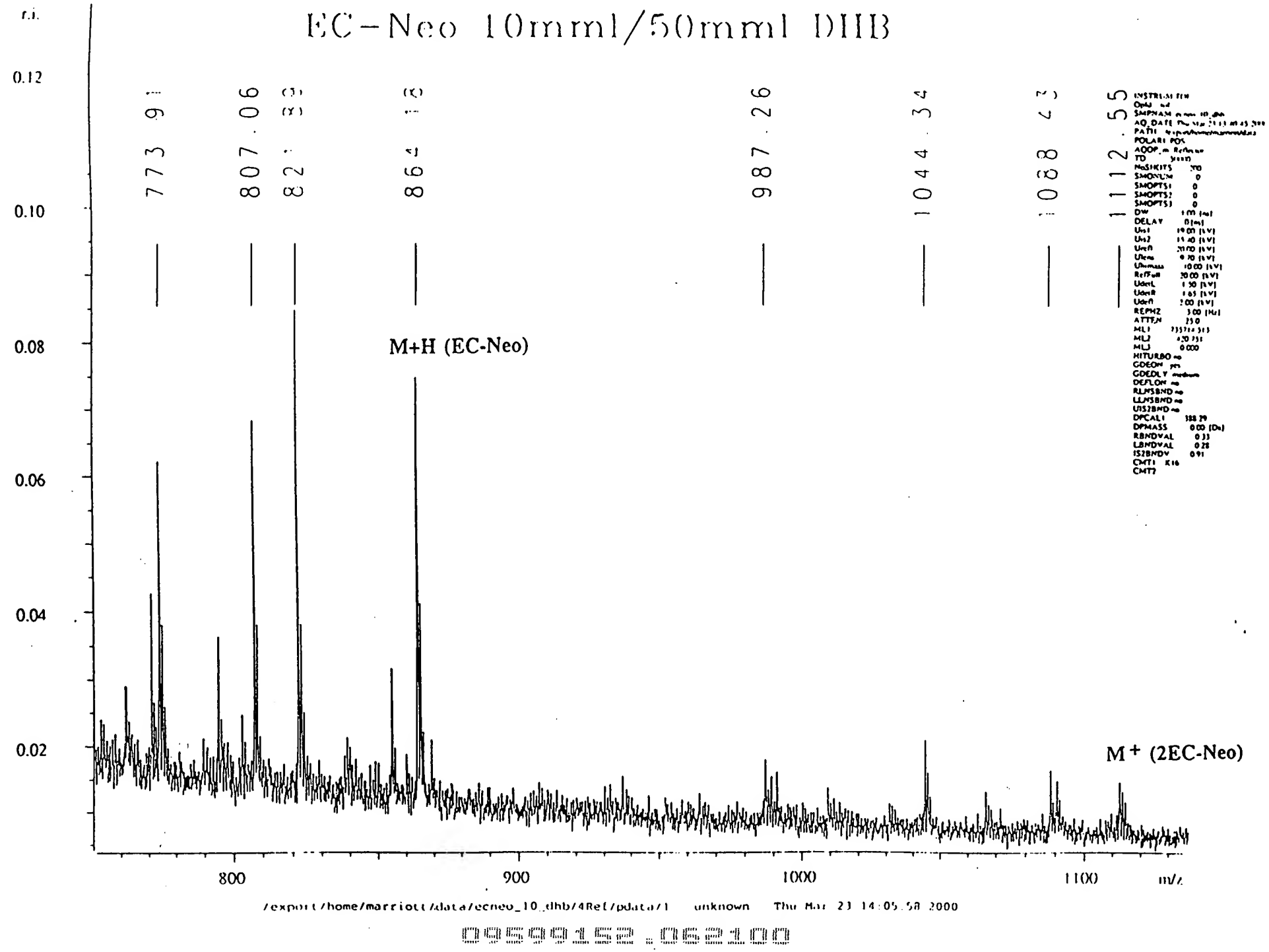


FIG. 39 Mass spectrometry of EC-neomycin (M^+ 1112.55).

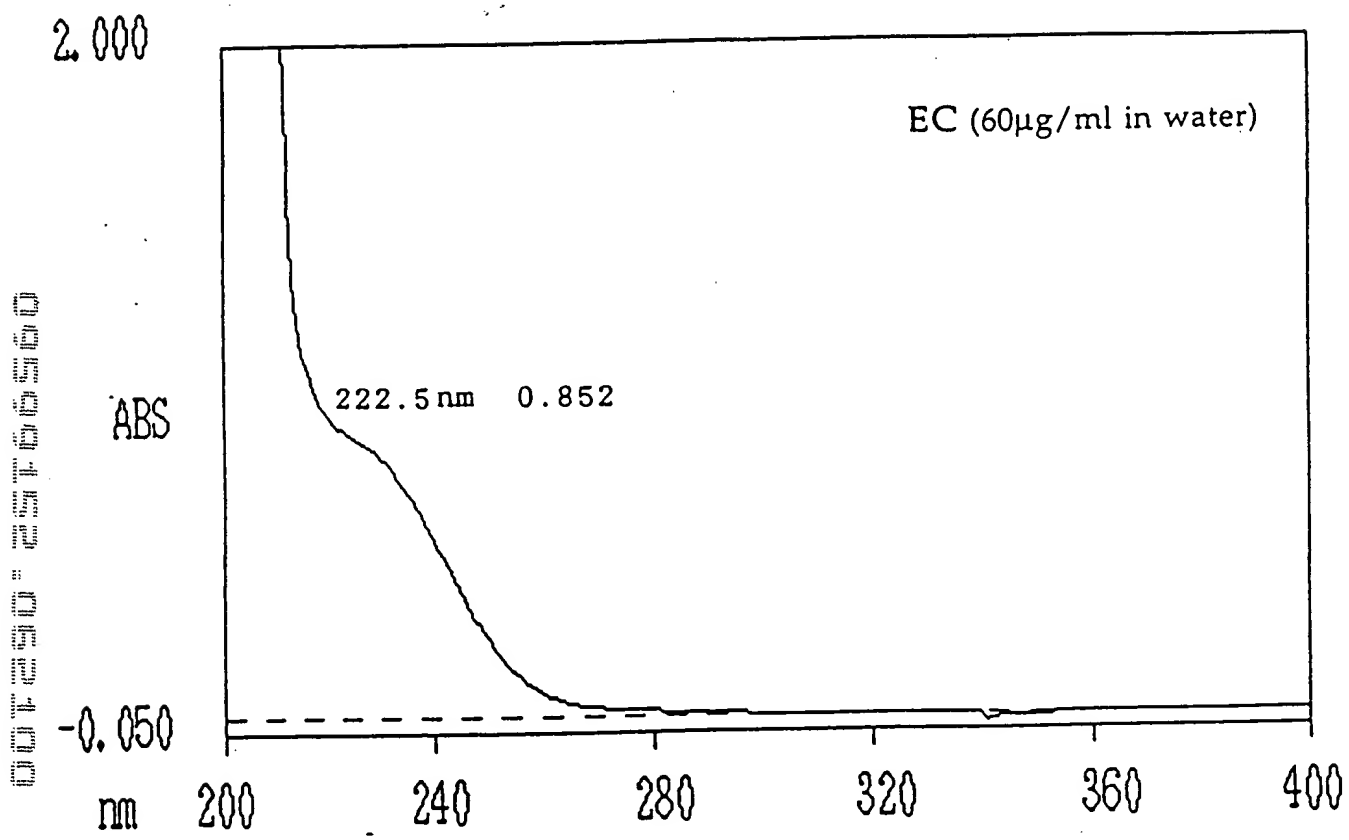


FIG. 40A

UV wavelength scan of EC.

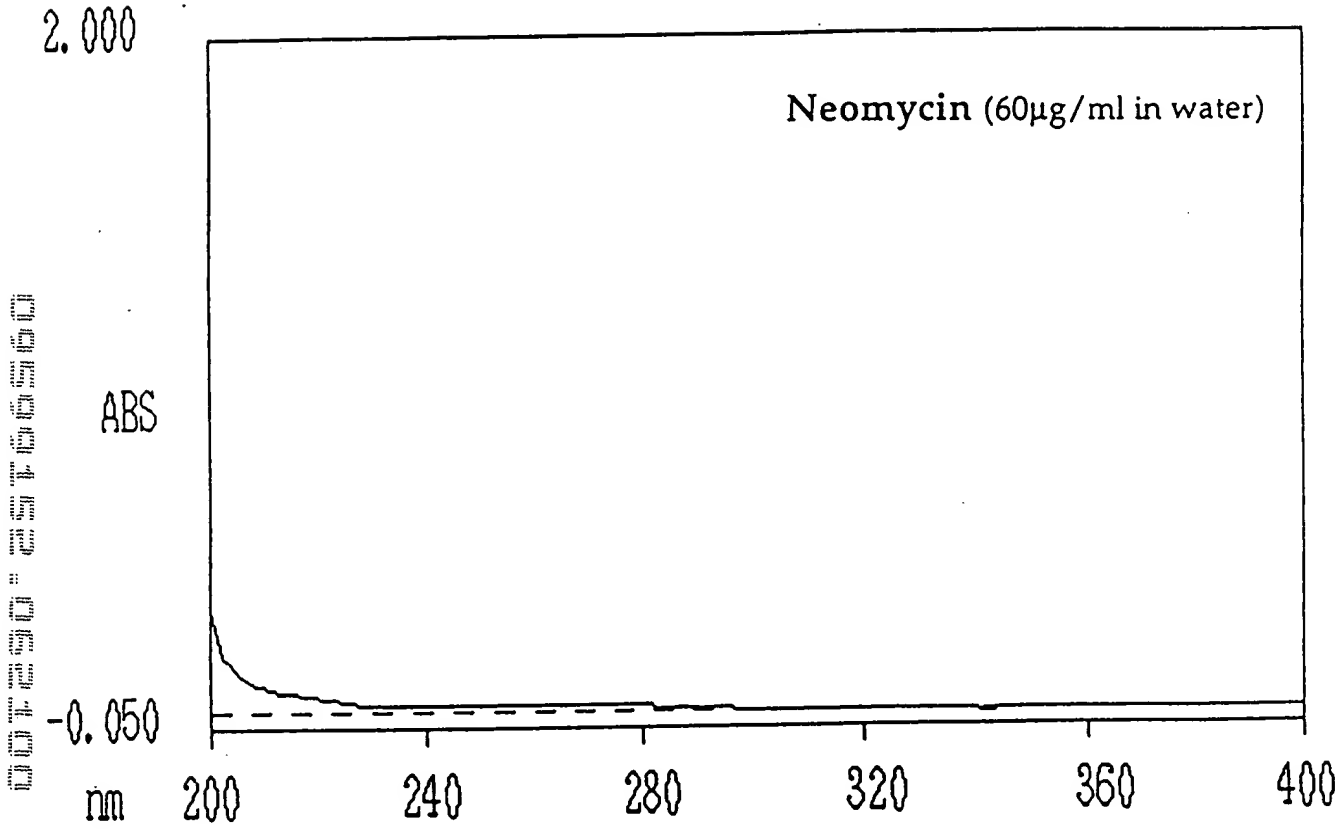


FIG. 40B UV wavelength scan of neomycin.

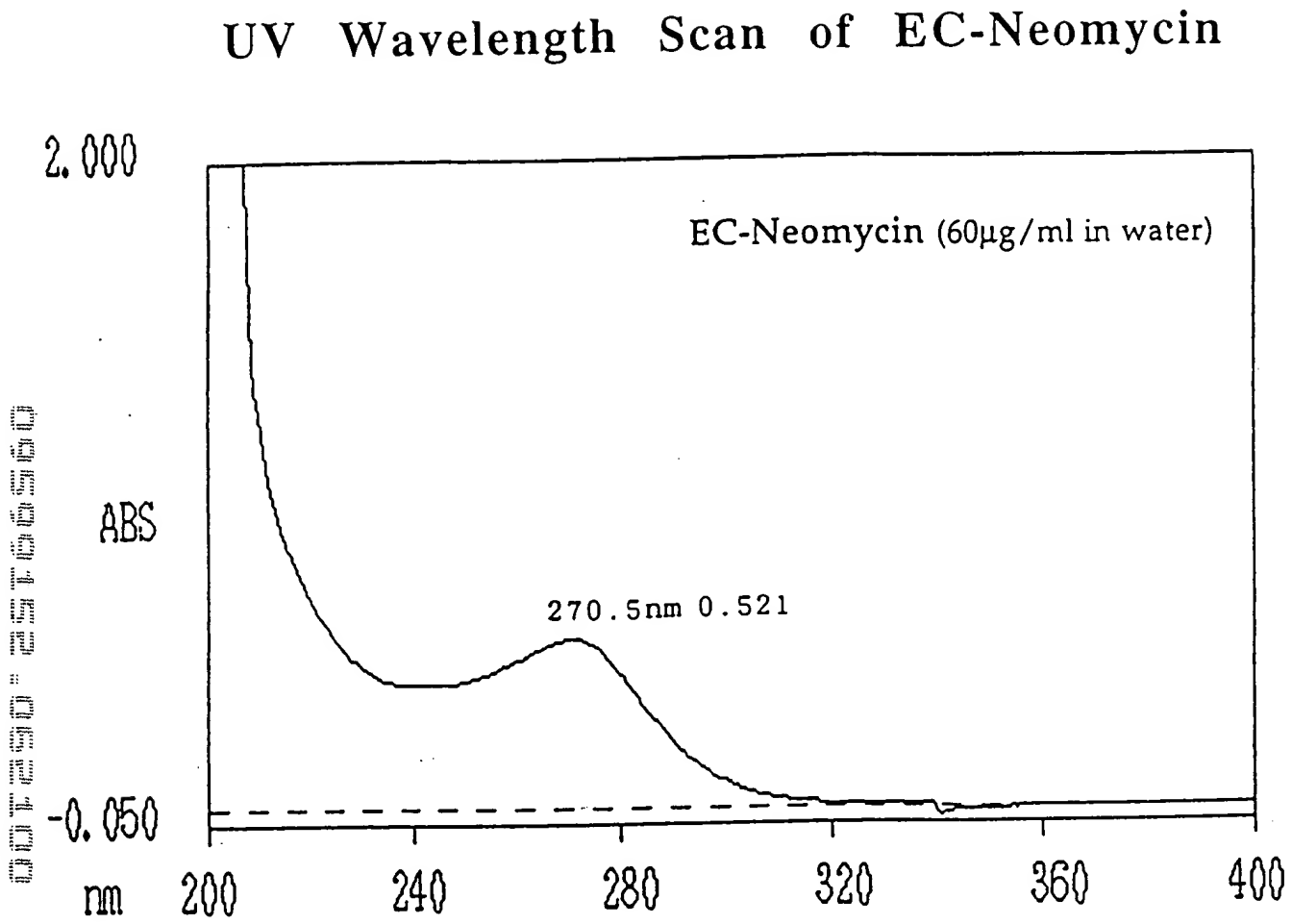


FIG. 40C UV wavelength scan of EC-neomycin.

SUMMARY REPORT

EC-NEOMYCIN 30mg + EC

Tc-99m
METHANOL-AMMONIUM ACETATE

Date: Feb 03 2000 Start time: 12:45 Accum time: 00:03:01
Data File: Plate: 1 Lane: 1

Elect Resolution: NORMAL (Amp. Range: 0 - 2047)
Rf Calculations: Origin: 0.00 cm Solvent Front: 20.00 cm
Integration Parameters: Auto Integration
Peak slope: 1.0 Min width: 0.1 Min %: 2.0

Total Count Region: 0.00cm to 20.00cm
Total Counts: 48360
Total CPM: 16030

Reg. #	Start (cm)	Stop (cm)	Center (cm)	Rf	Region Counts	Region CPM	% of Tot Reg	% of Tot Cnt
1	6.50	14.90	10.57	0.53	45000	14920	100.00	93.05
TOTAL					45000	14920	100.00	93.05

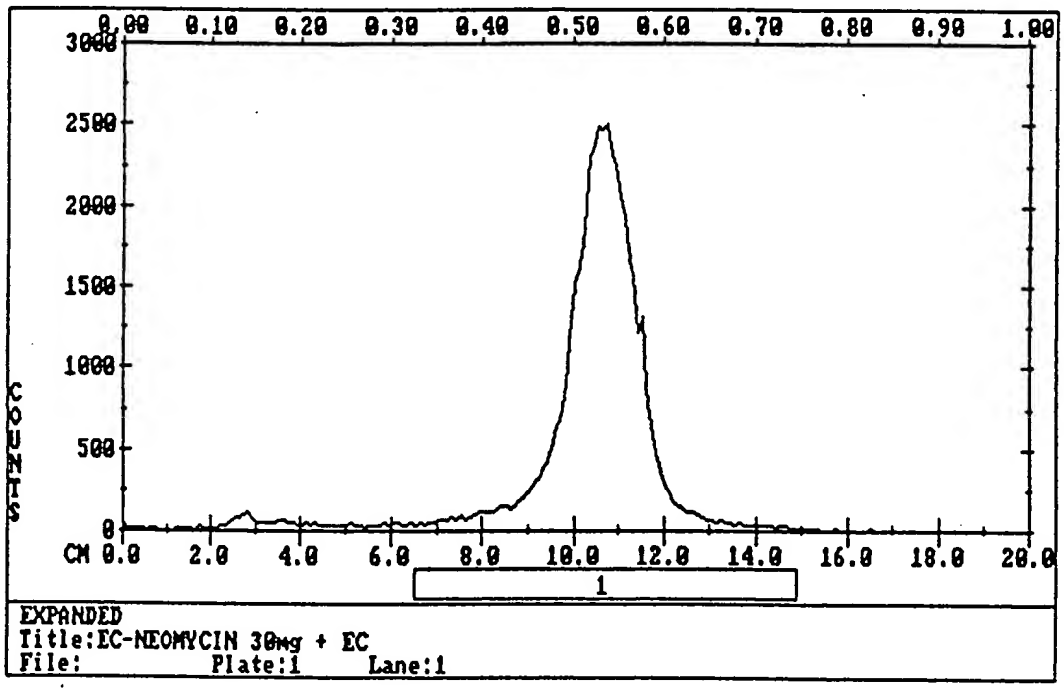


FIG. 41 Radio-TLC analysis of ^{99m}Tc-EC-neomycin.

^{99m}Tc-EC-NEO

Column: Bio-Rad Carbohydrate, Aminex HPX-87C, 250x4mm

Eluent: H_2O

Flow Rate: 0.4ml/min

Detector: Radiochemical

Temp: 85.0°C

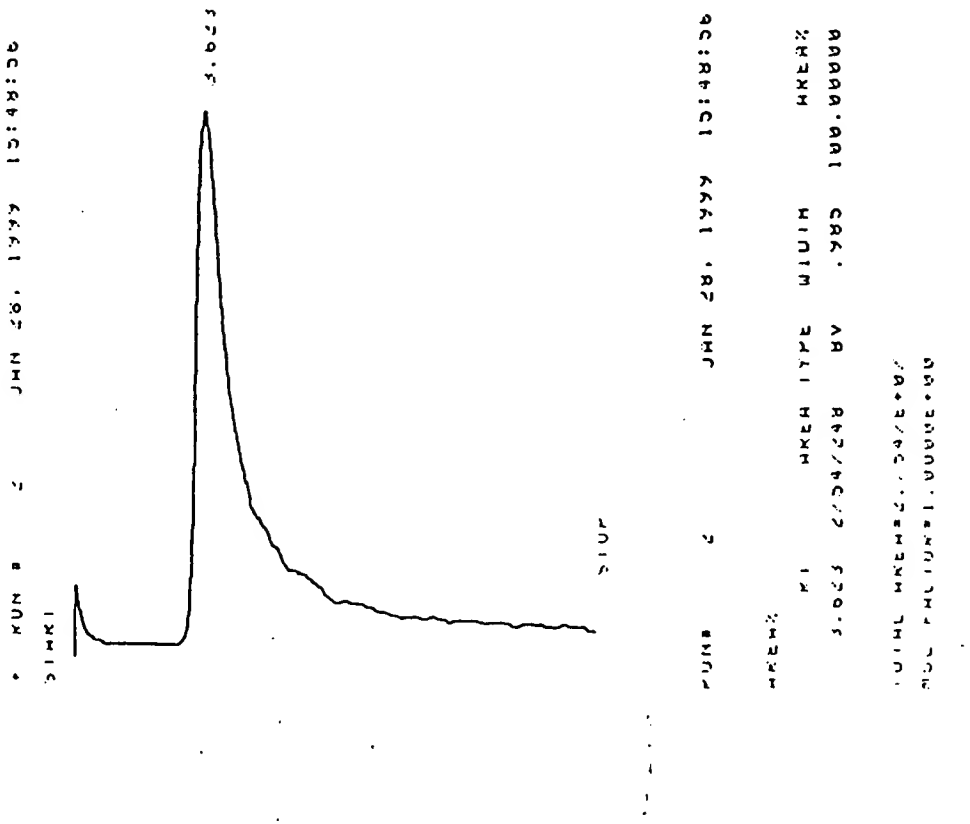


FIG. 42 HPLC analysis of ^{99m}Tc-EC-neomycin (radioactive detector).

^{99m}Tc-EC-NEO

Column: Bio-Rad Carbohydrate, Aminex HPX-87C, 250x4mm

Eluent: H_2O

Flow Rate: 0.4ml/min

Detector: UV, 254nm

Temp: 85.0°C

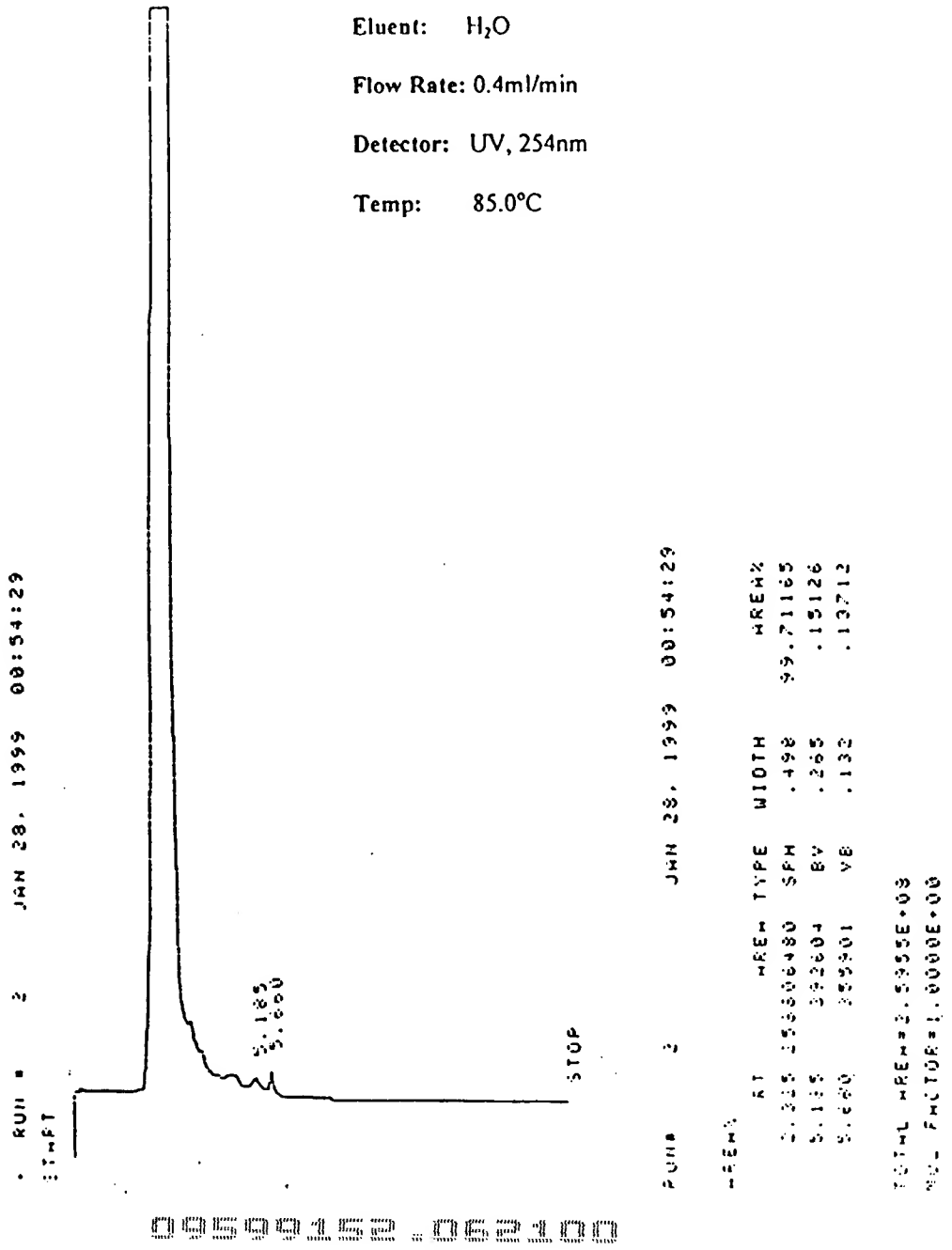
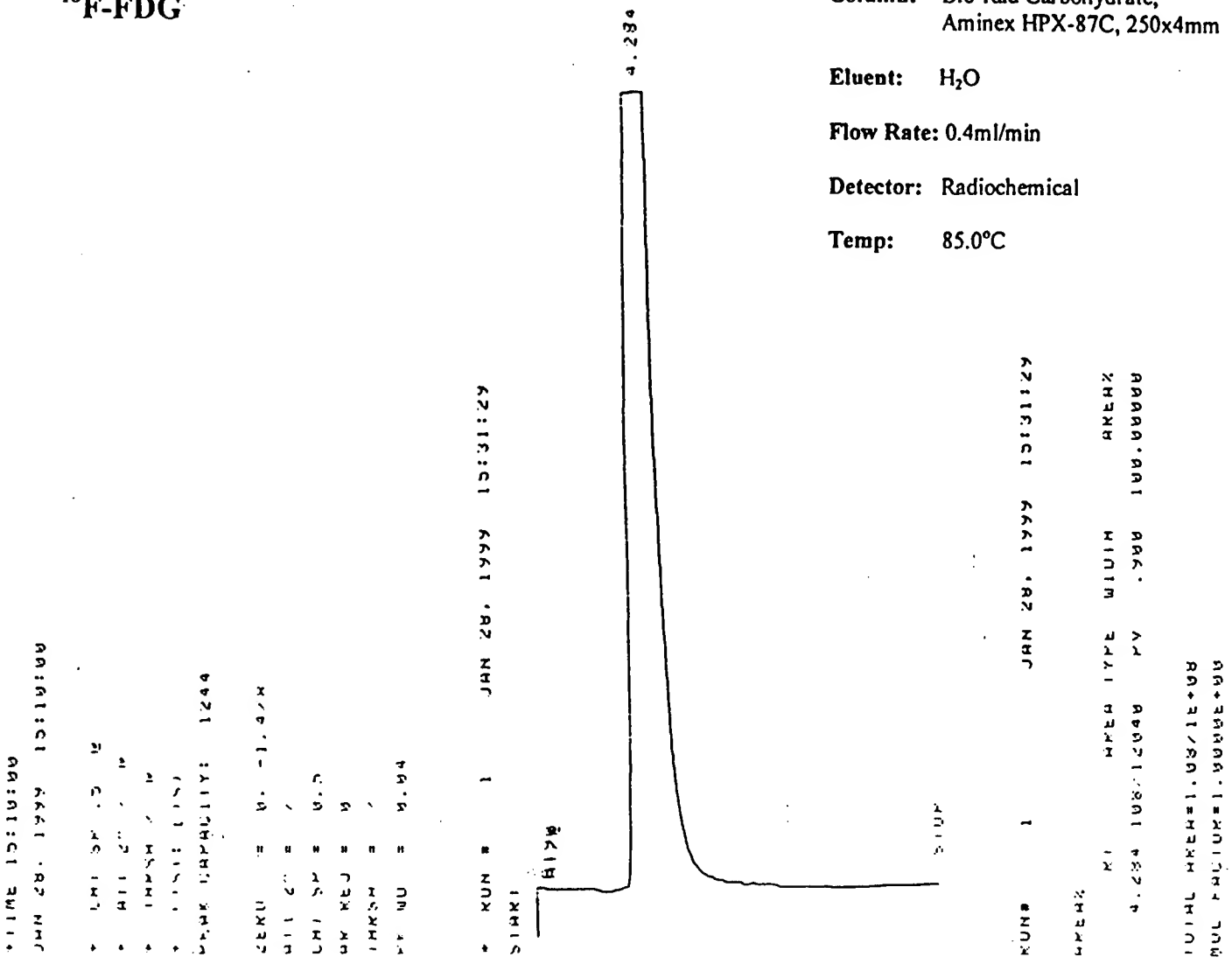


FIG. 43 HPLC analysis of ^{99m}Tc-EC-neomycin (UV 254 nm).

^{18}F-FDG



Column: Bio-Rad Carbohydrate, Aminex HPX-87C, 250x4mm

Eluent: H_2O

Flow Rate: 0.4ml/min

Detector: Radiochemical

Temp: 85.0°C

FIG. 44 HPLC analysis of ^{18}F-FDG (radioactive detector).

^{18}F-FDG

Column: Bio-Rad Carbohydrate, Aminex HPX-87C, 250x4mm

Eluent: H_2O

Flow Rate: 0.4ml/min

Detector: UV, 254nm

Temp: 85.0°C

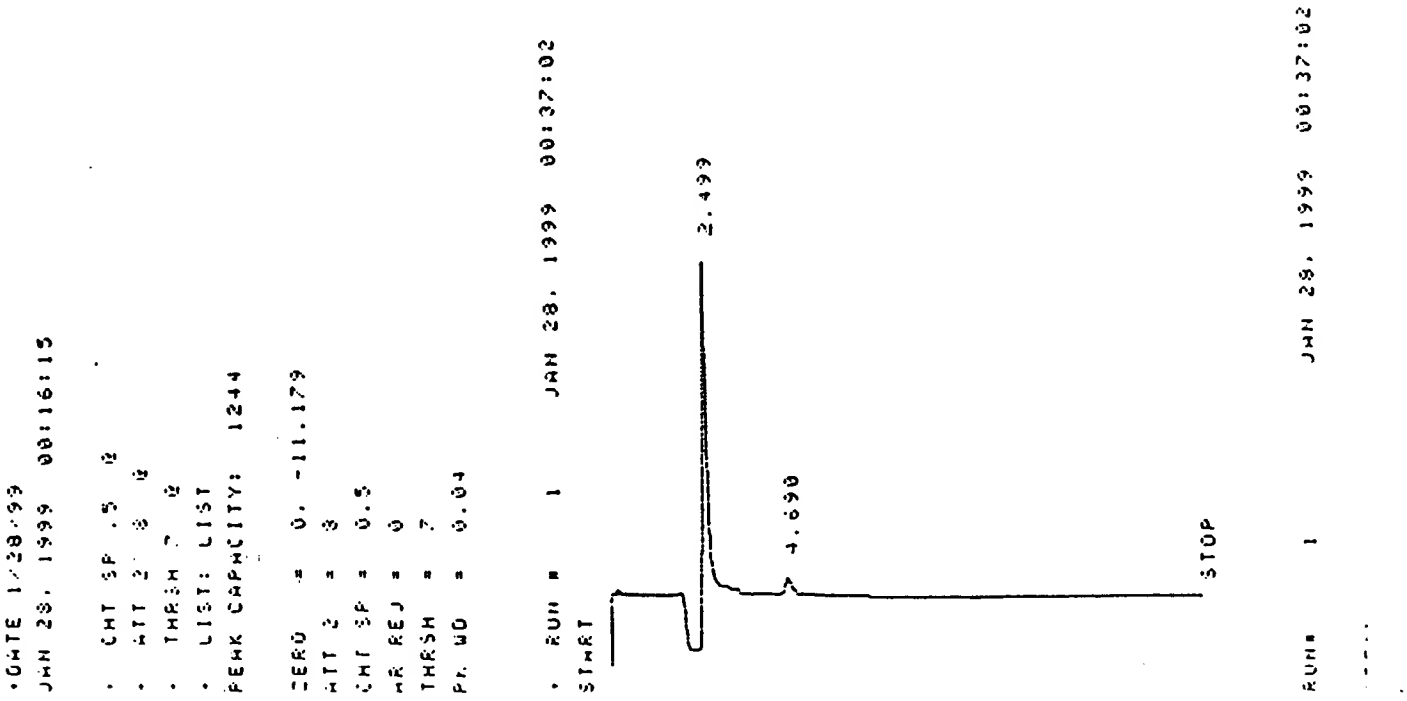


FIG. 45 HPLC analysis of ^{18}F-FDG (UV 254 nm).

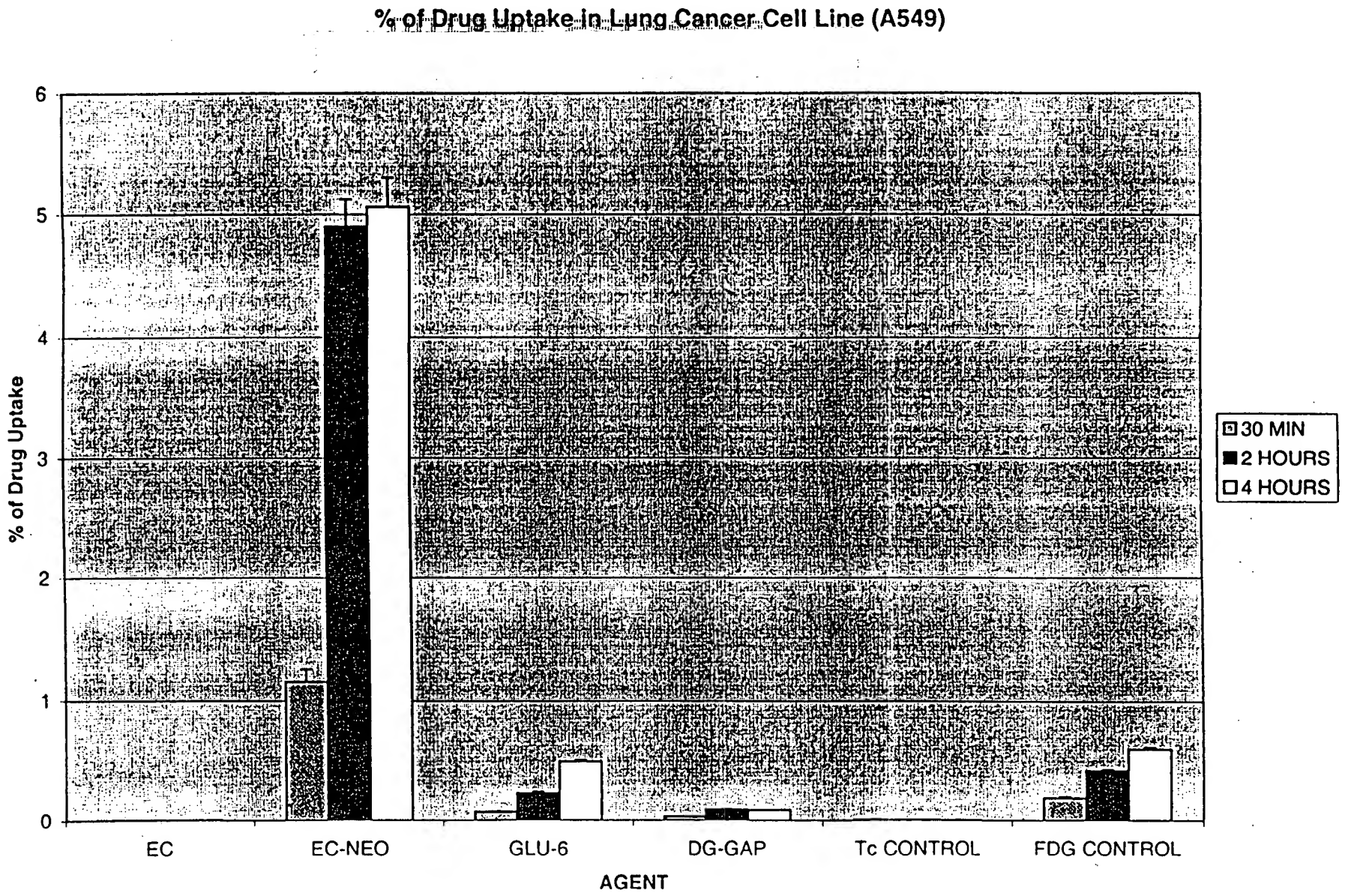


FIG. 46 In vitro cellular uptake assay of a series of ^{99m}Tc-EC-drug conjugates in lung cancer cell line. ^{99m}Tc-EC- neomycin showed highest uptake in the agents tested.

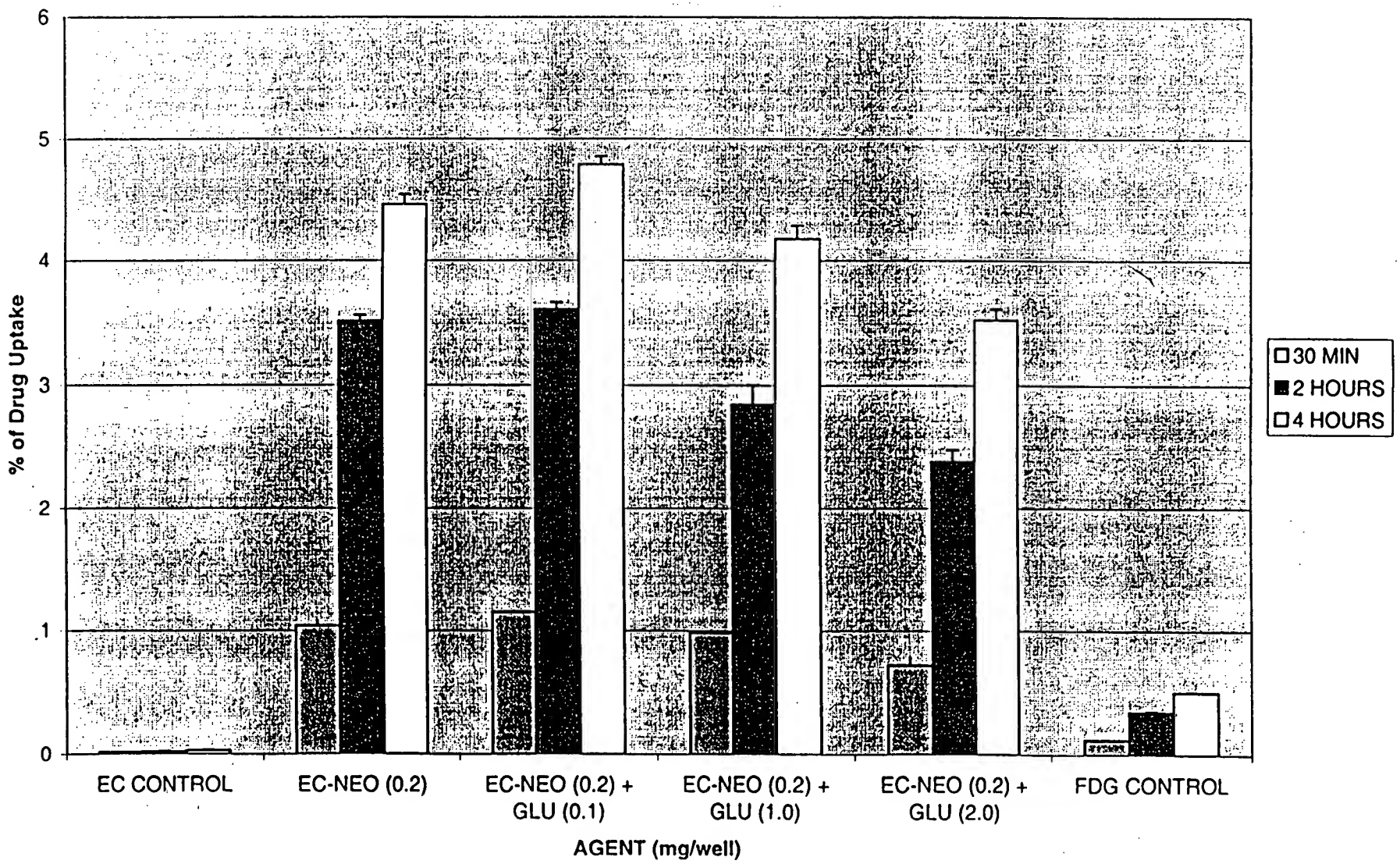


FIG. 47 Effect of glucose on cellular (A549) uptake of ^{99m}Tc-EC- neomycin and ^{18}F-FDG.

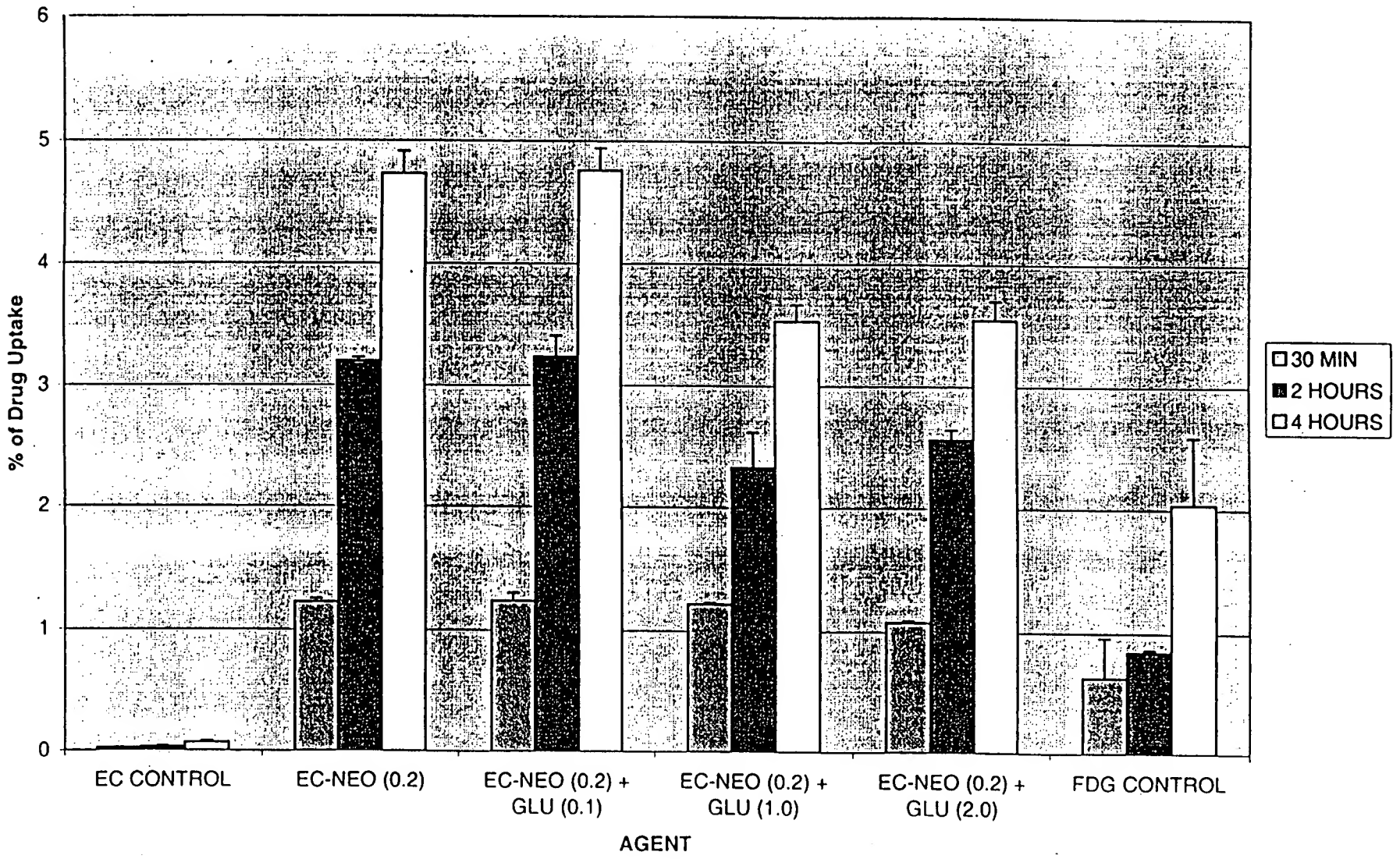


FIG. 48A

Effect of glucose on cellular (H11299) uptake of ^{99m}Tc-EC-neomycin and ^{18}F-FDG.

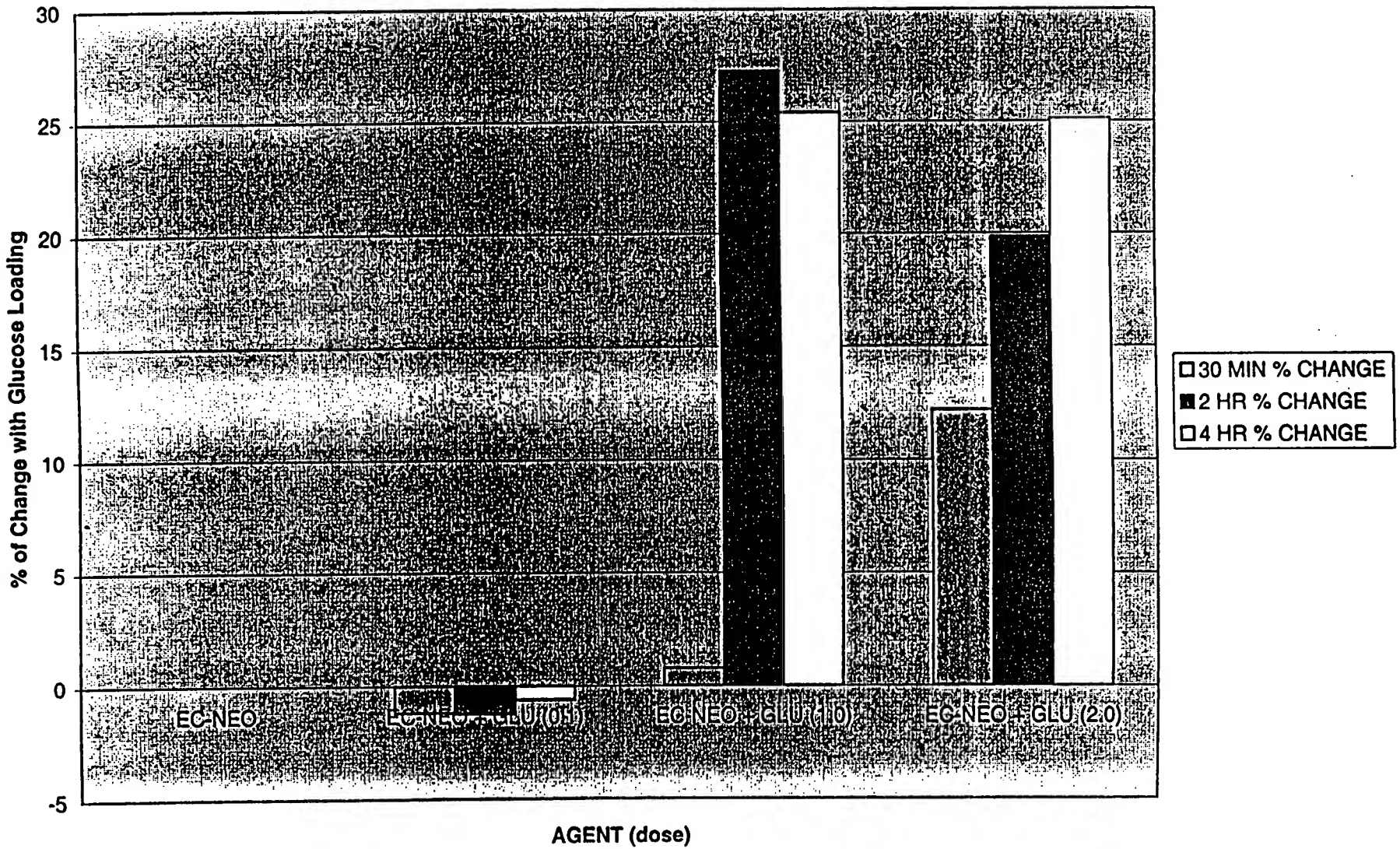
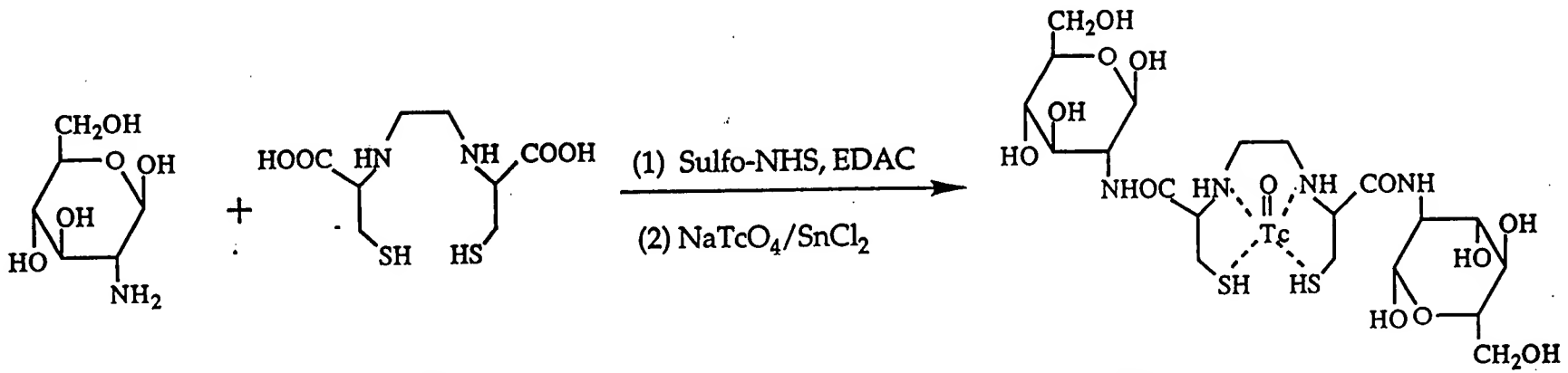


FIG. 48B



D(+)-Glucosamine EC ^{99m}Tc-EC-Glucosamine

FIG. 49 Synthesis of ^{99m}Tc-EC-Glucosamine

Hexokinase Assay of Glucose

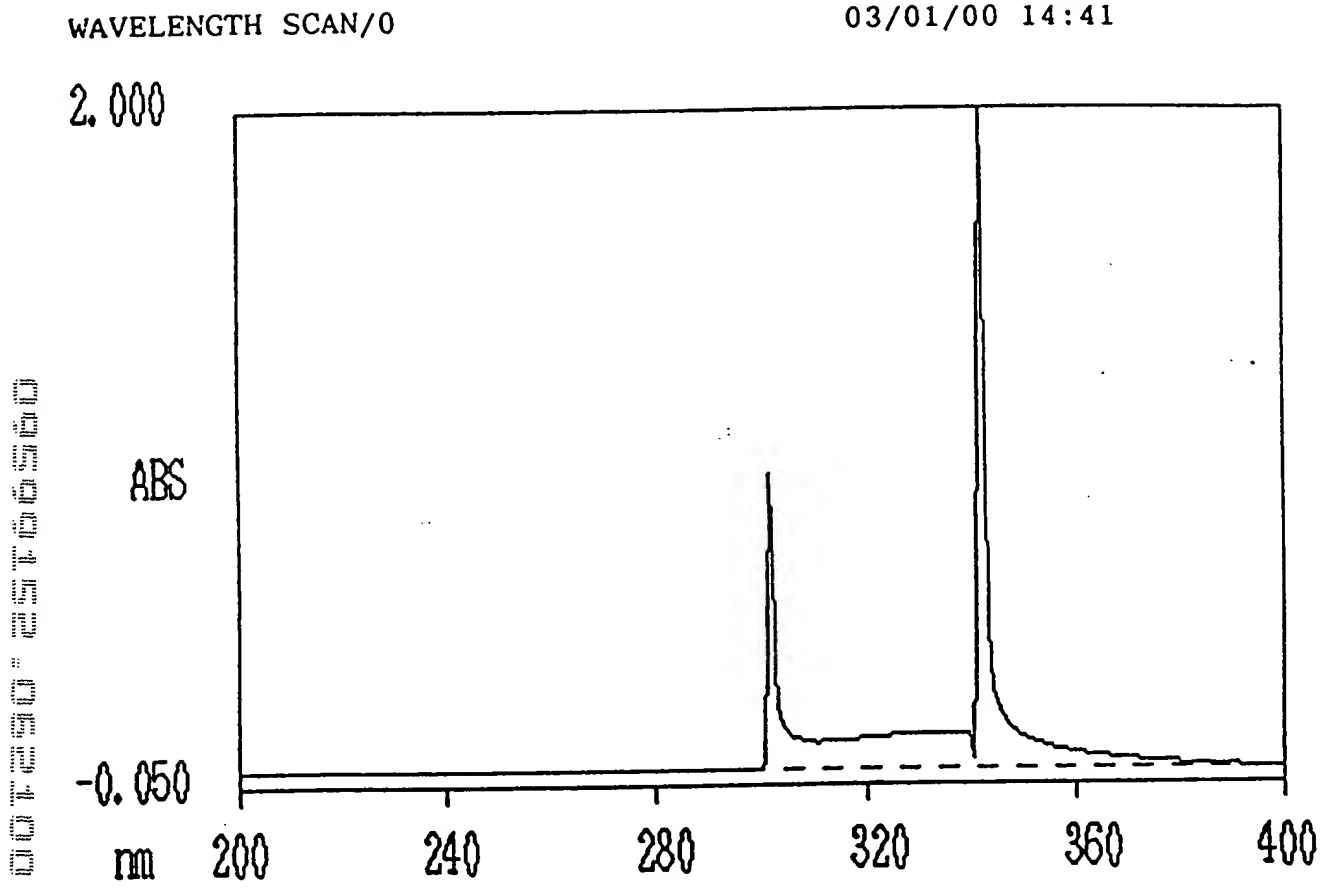


FIG. 50

Hexokinase Assay of Glucosamine

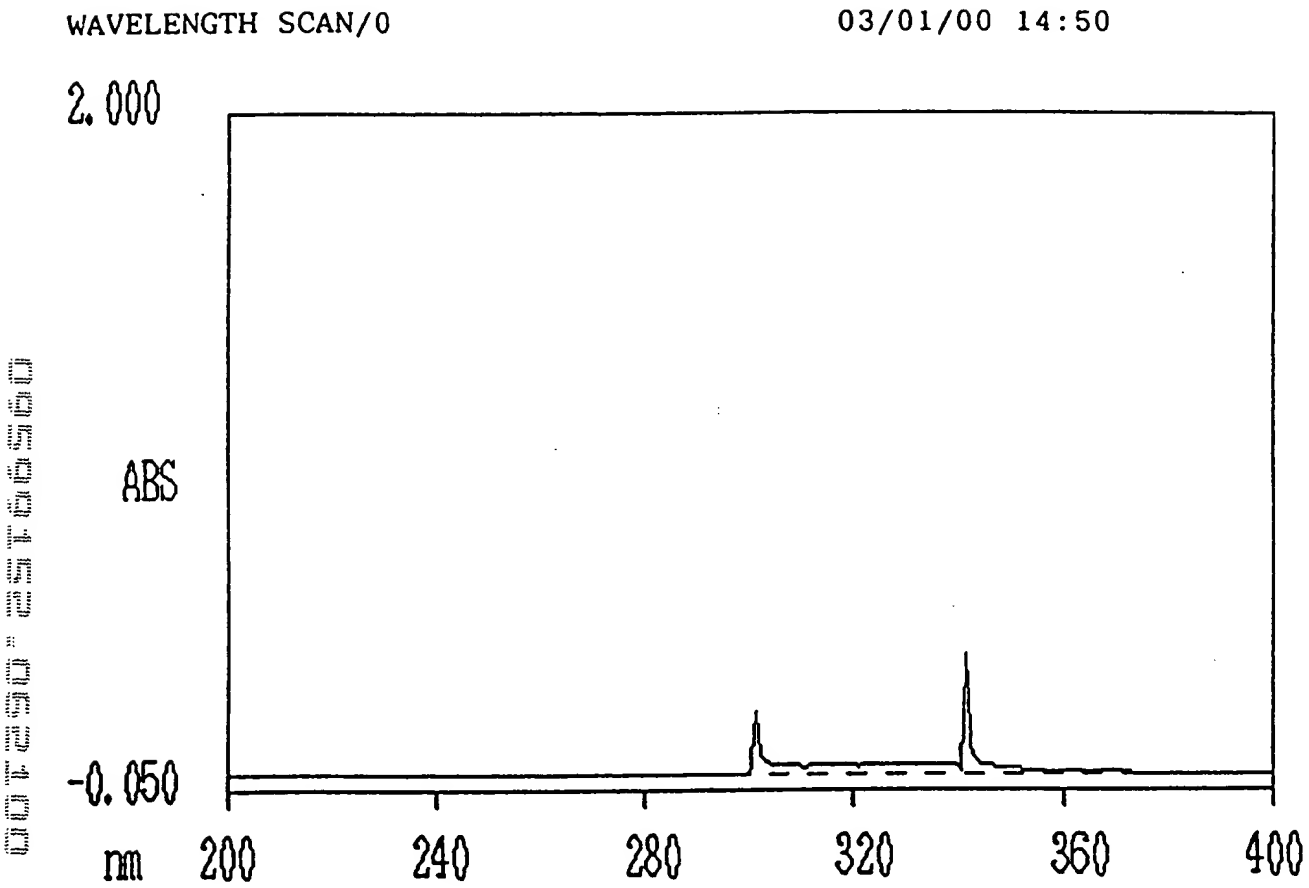


FIG. 51

Hexokinase Assay of EC-Glucosamine

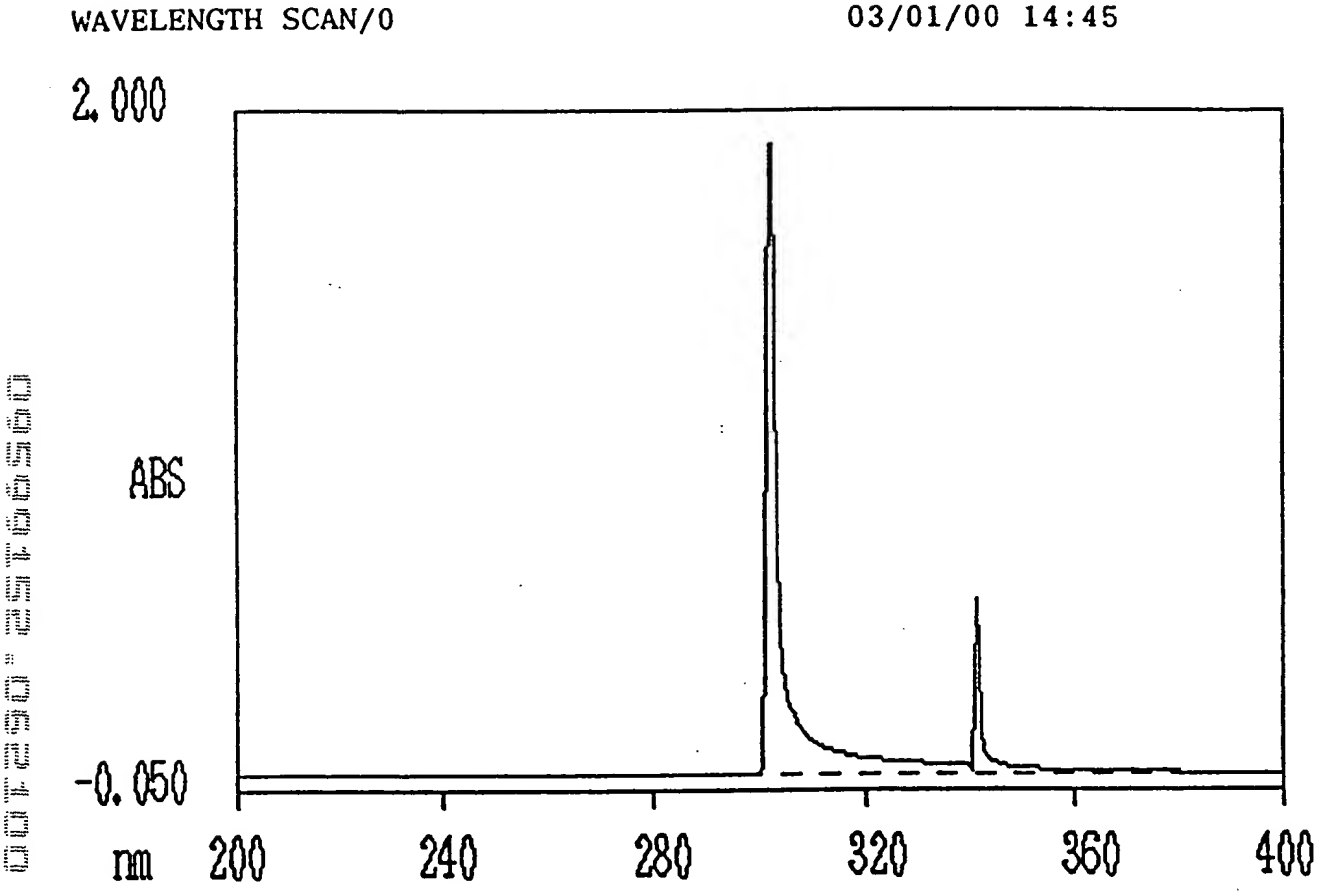


FIG. 52

Hexokinase Assay of EC-GAP-Glucosamine

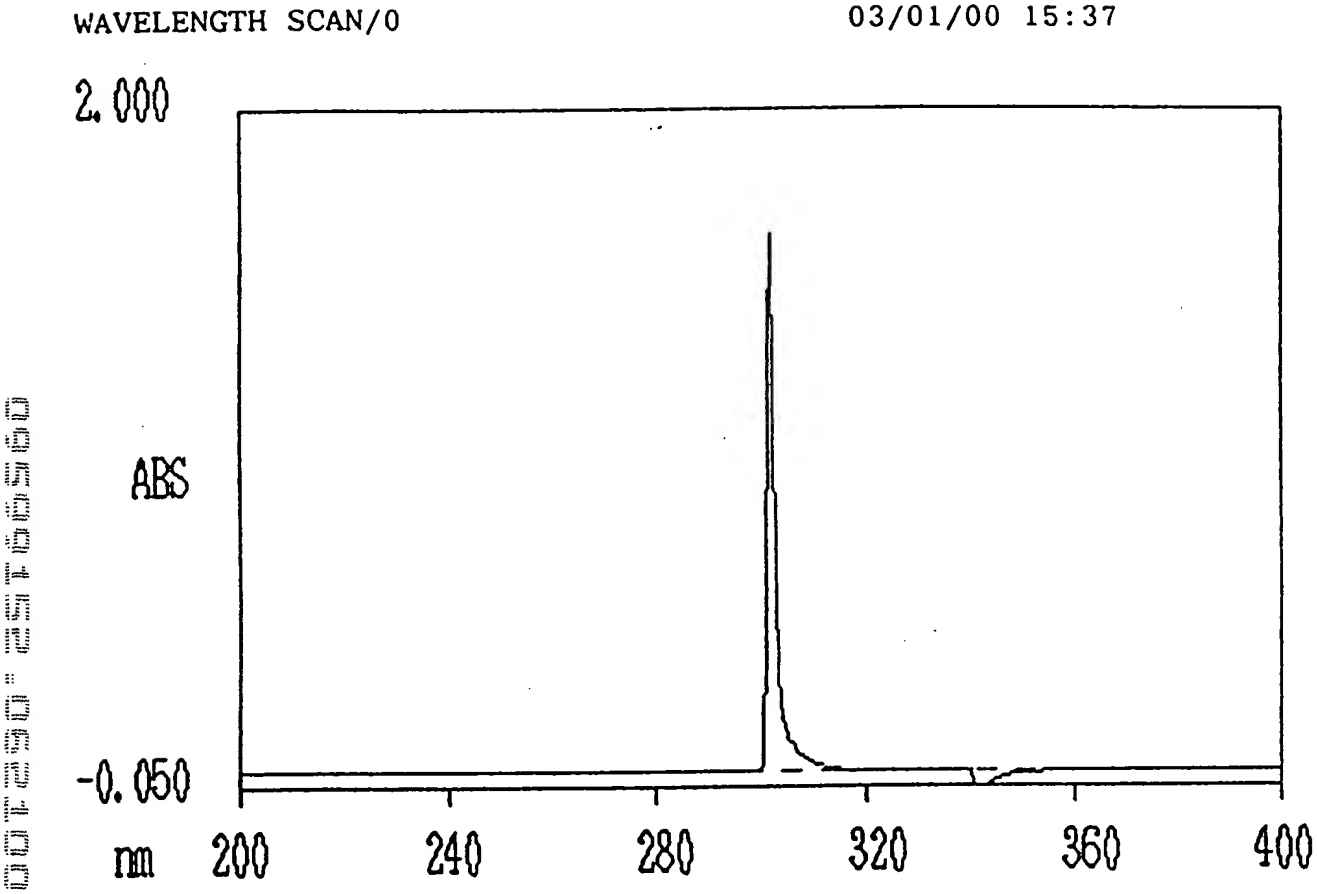
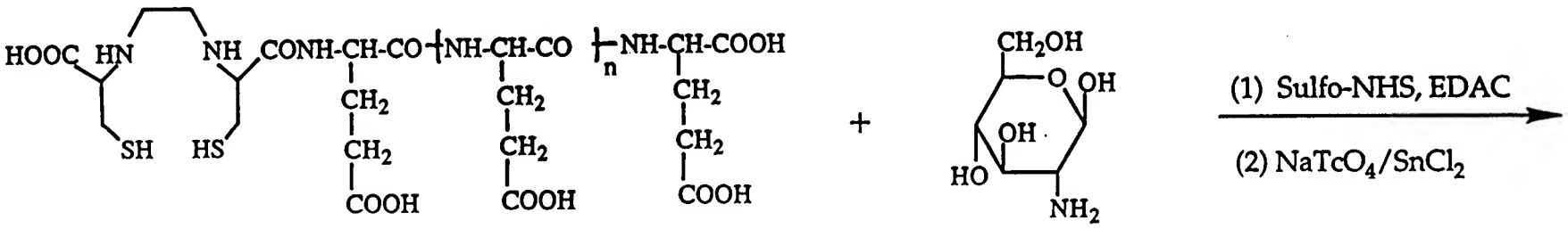
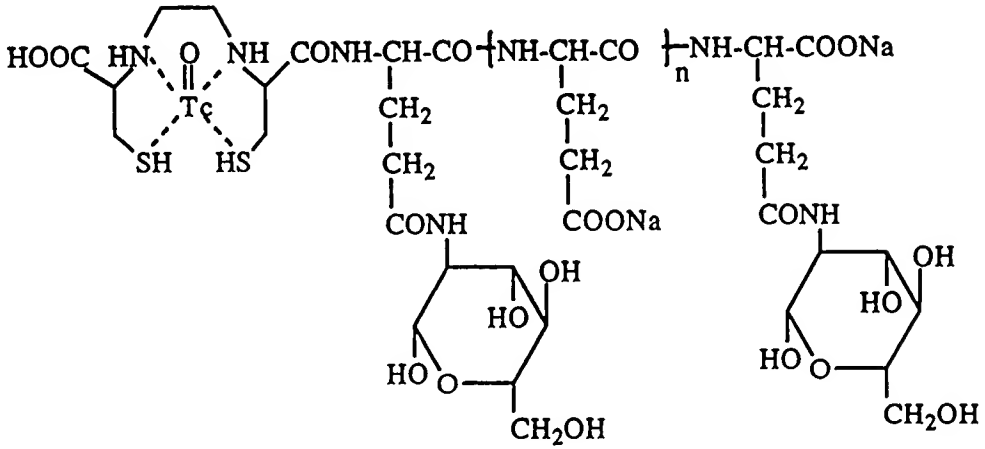


FIG. 53



EC-GAP

D(+)-Glucosamine



^{99m}Tc-EC-GAP-Glucosamine

FIG. 54 Synthesis of ^{99m}Tc-EC-GAP-Glucosamine

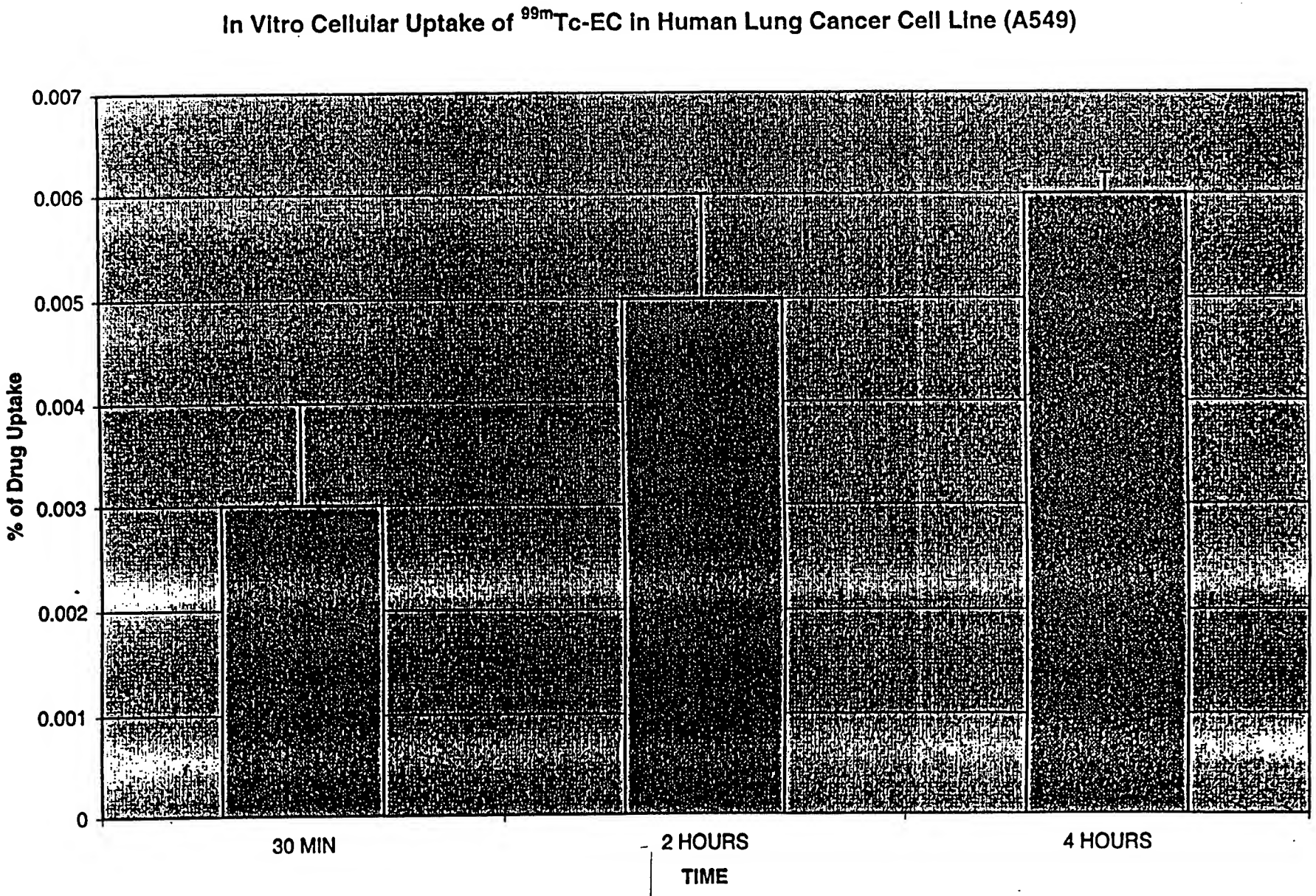
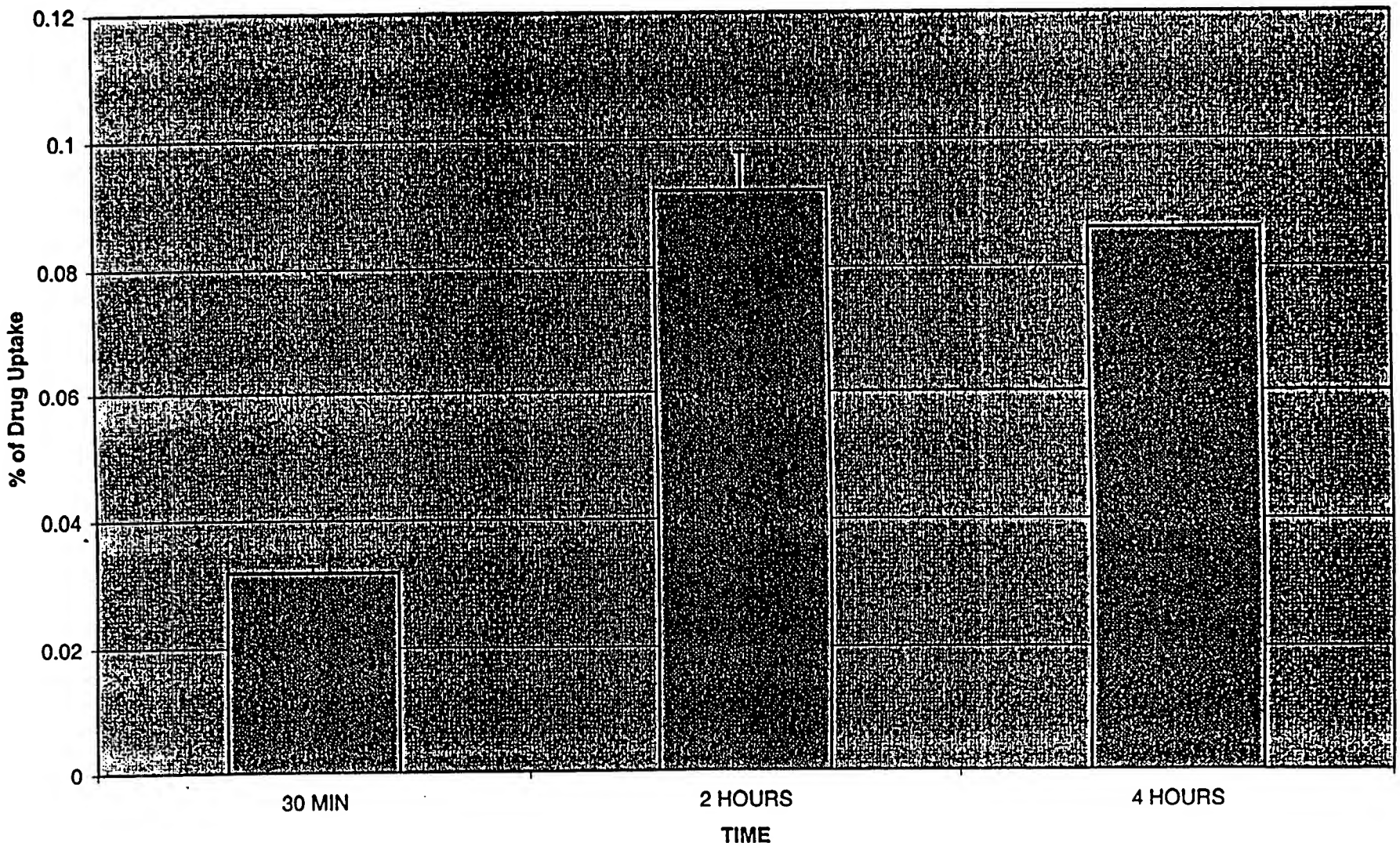

In Vitro Cellular Uptake of 99mTc-EC in Human Lung Cancer Cell Line (A549)
0.007
0.006
0.005
0.004
0.003
0.002
0.001
0
% of Drug Uptake
30 MIN
2 HOURS
4 HOURS
TIME

FIG. 55A



0959152 . 062100

FIG. 55B

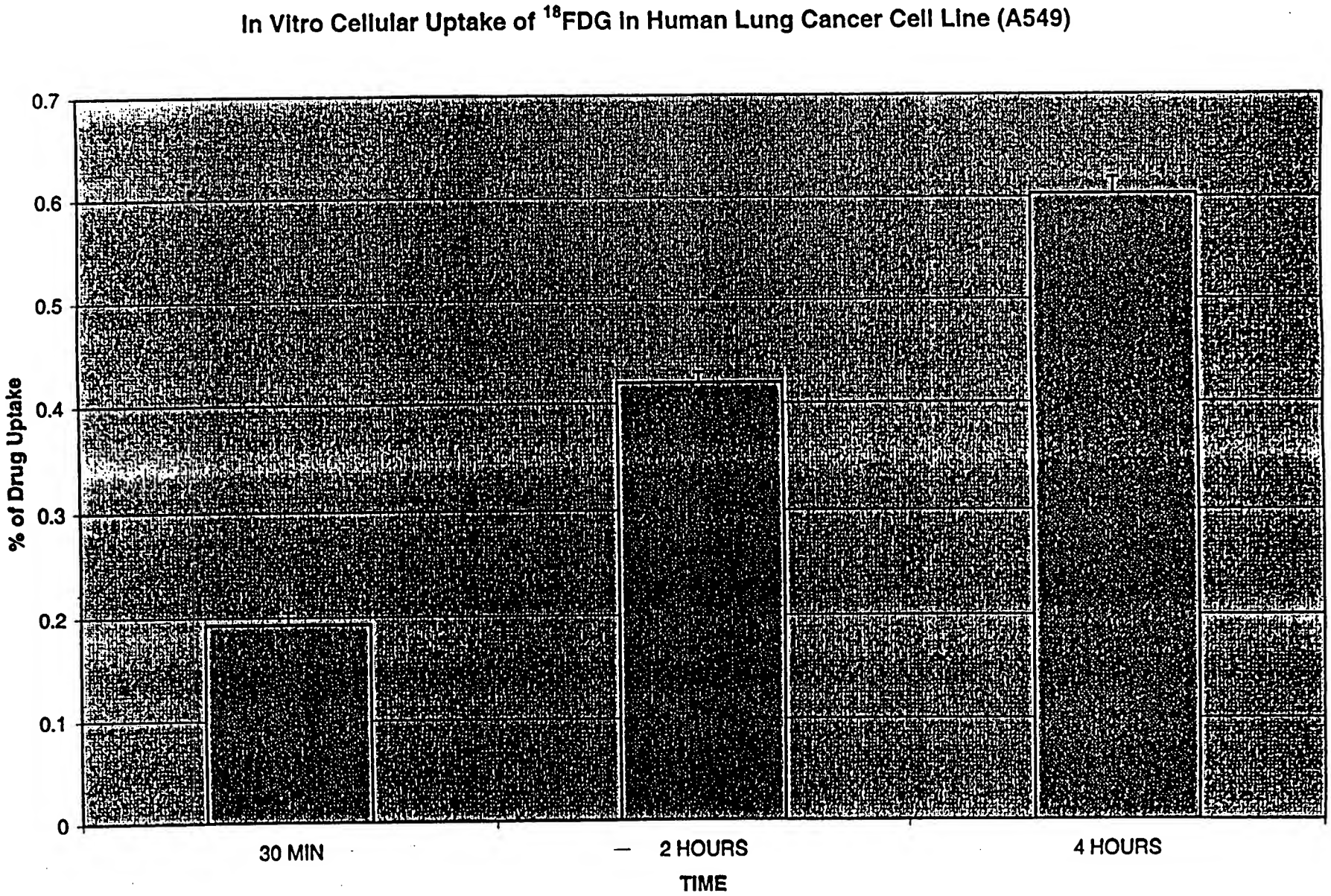


FIG. 55C

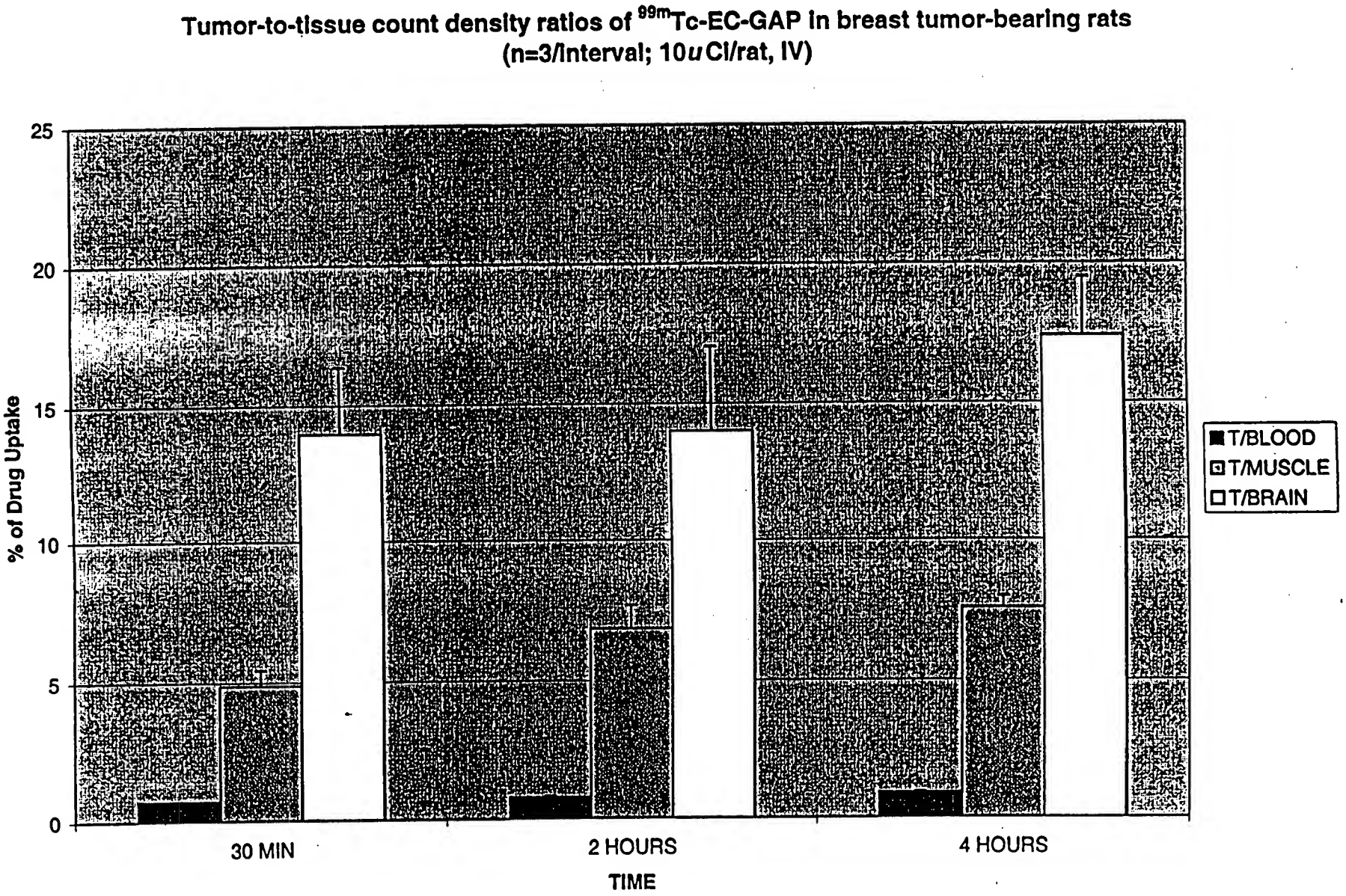


FIG. 56

In Vitro Cellular Uptake of ^{18}FDG with Glucose Loading at 2 Hours Post-Injection in Breast Cancer Cell Line (13762)

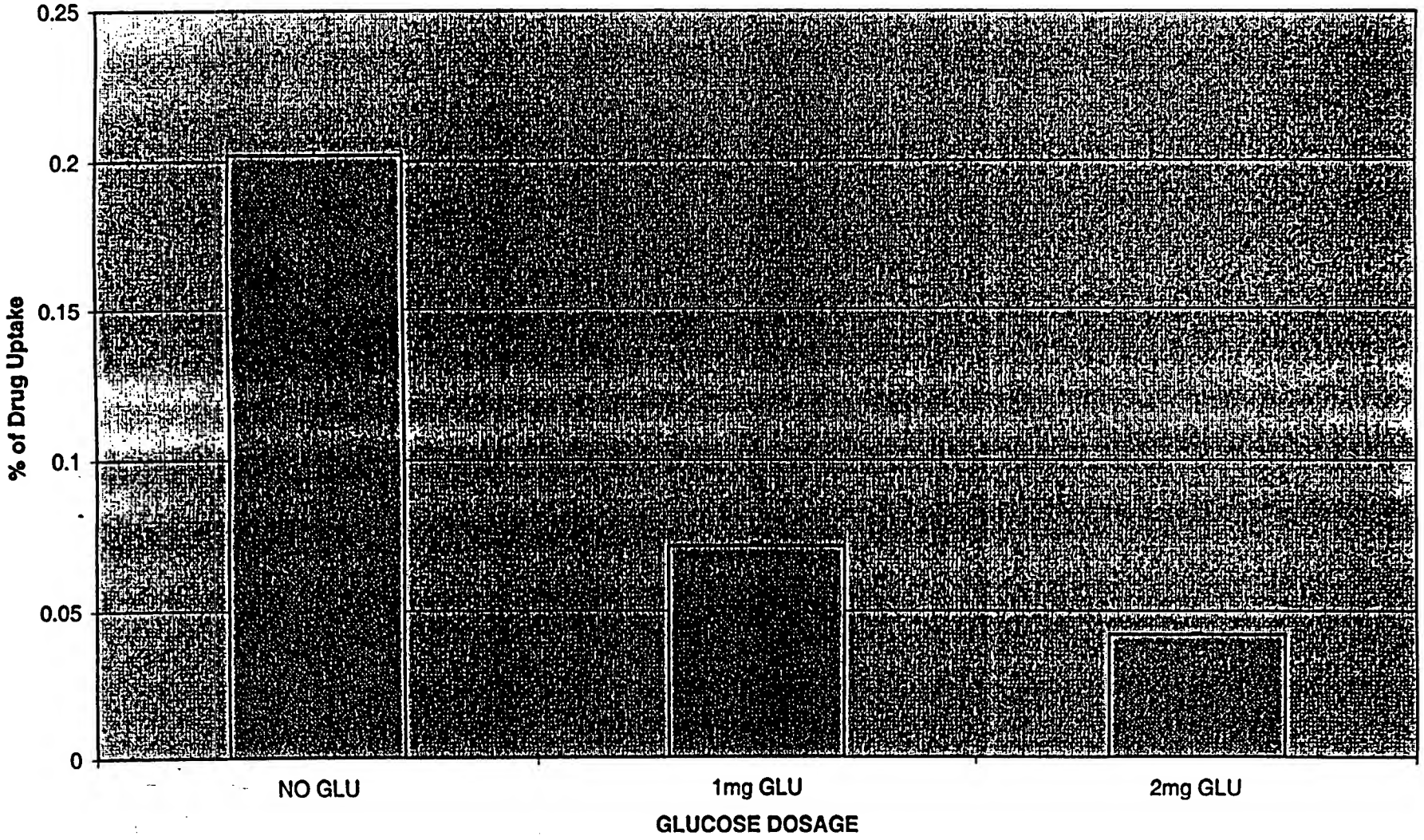


FIG. 57

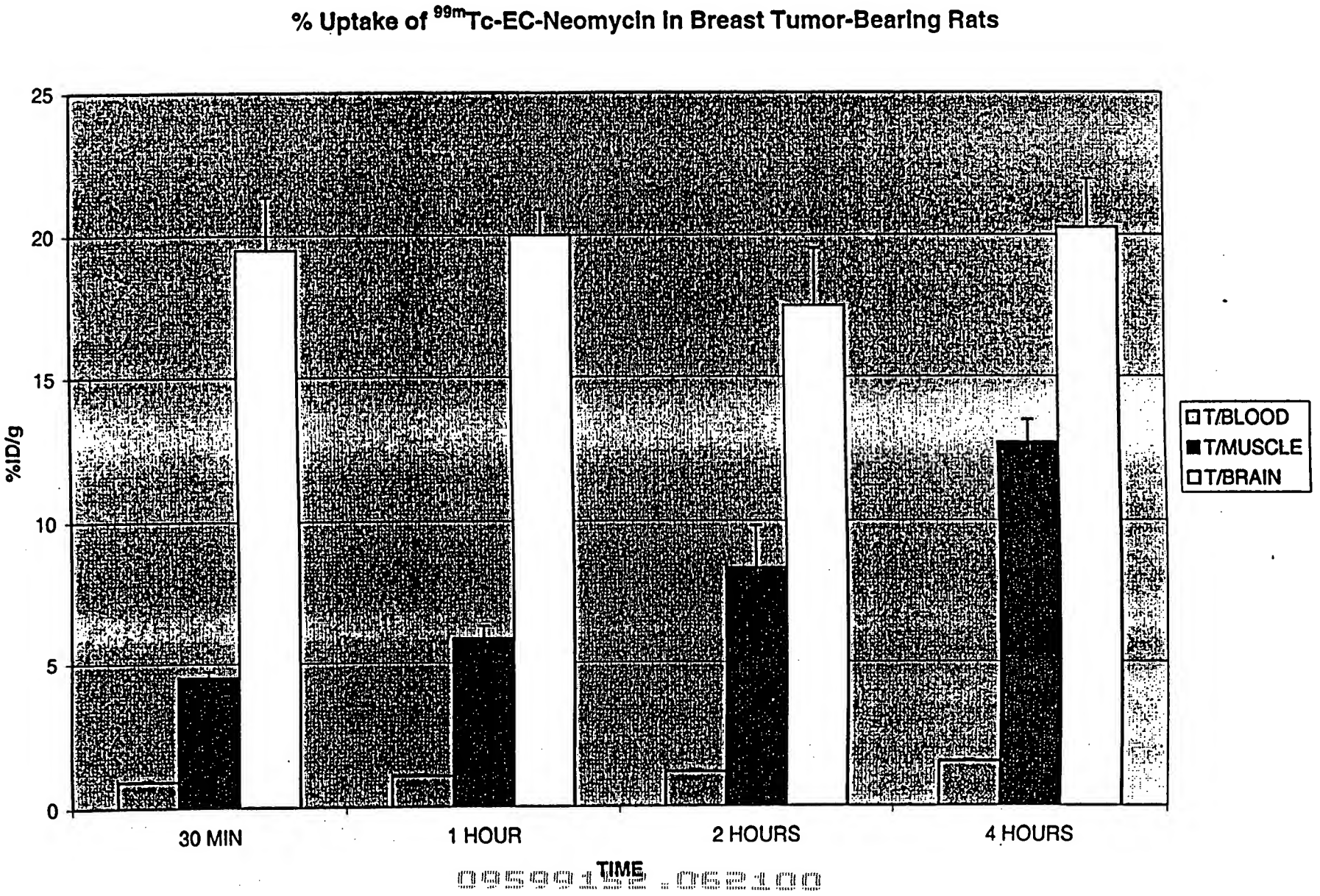

% Uptake of 99mTc-EC-Neomycin In Breast Tumor-Bearing Rats
25
20
15
10
5
0
%ID/g
30 MIN
1 HOUR
2 HOURS
4 HOURS
TIME
T/BLOOD
T/MUSCLE
T/BRAIN

FIG. 58

D(+)-Glucosamine **EC** **^{99m}Tc-EC-Glucosamine**

FIG. 59 Synthetic scheme of ^{99m}Tc-EC-deoxyglucose.

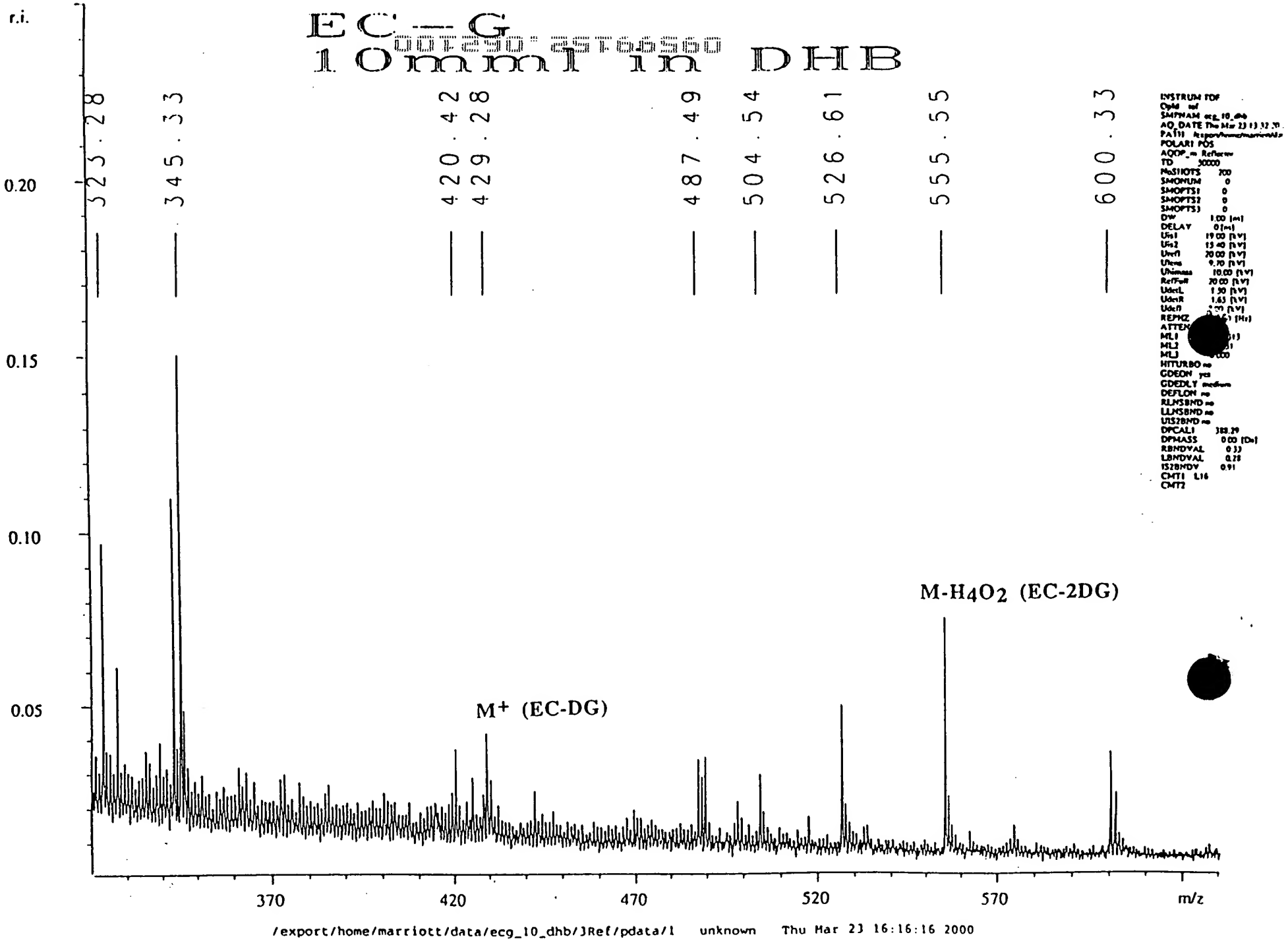


FIG. 60 Mass spectrometry of EC-deoxyglucose.

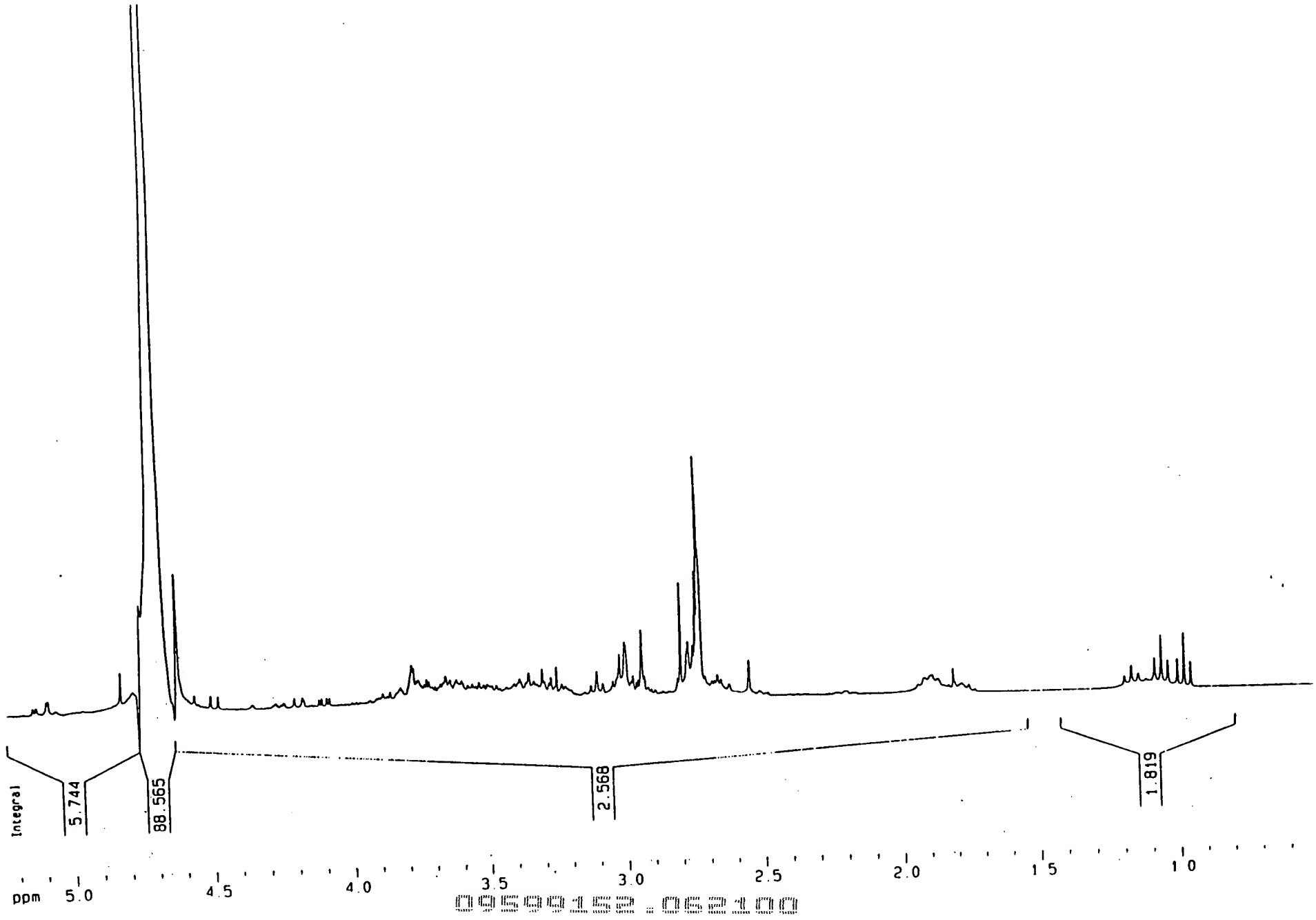


FIG. 61 ^{1}H-NMR of EC-deoxyglucose (EC-DG).

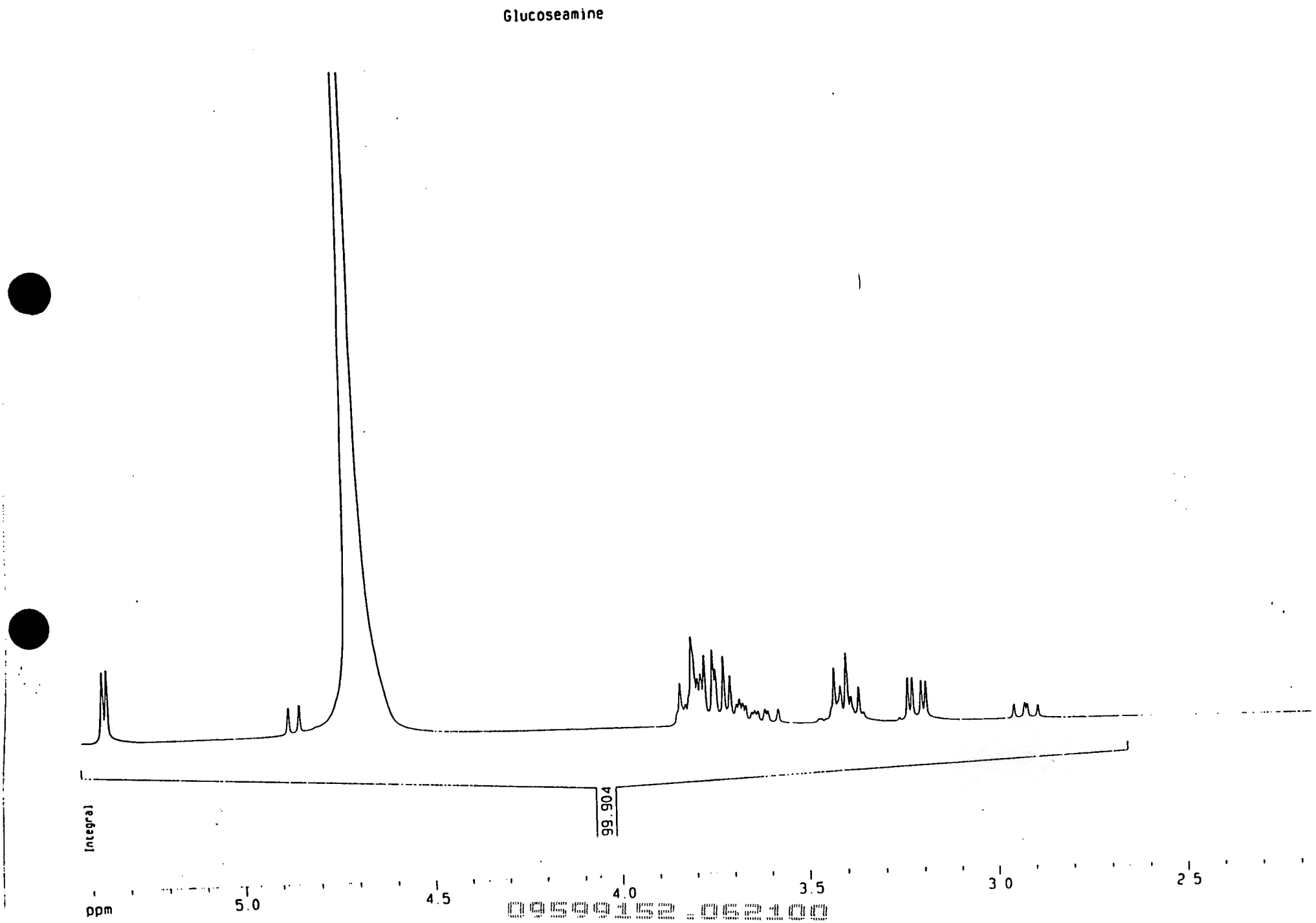
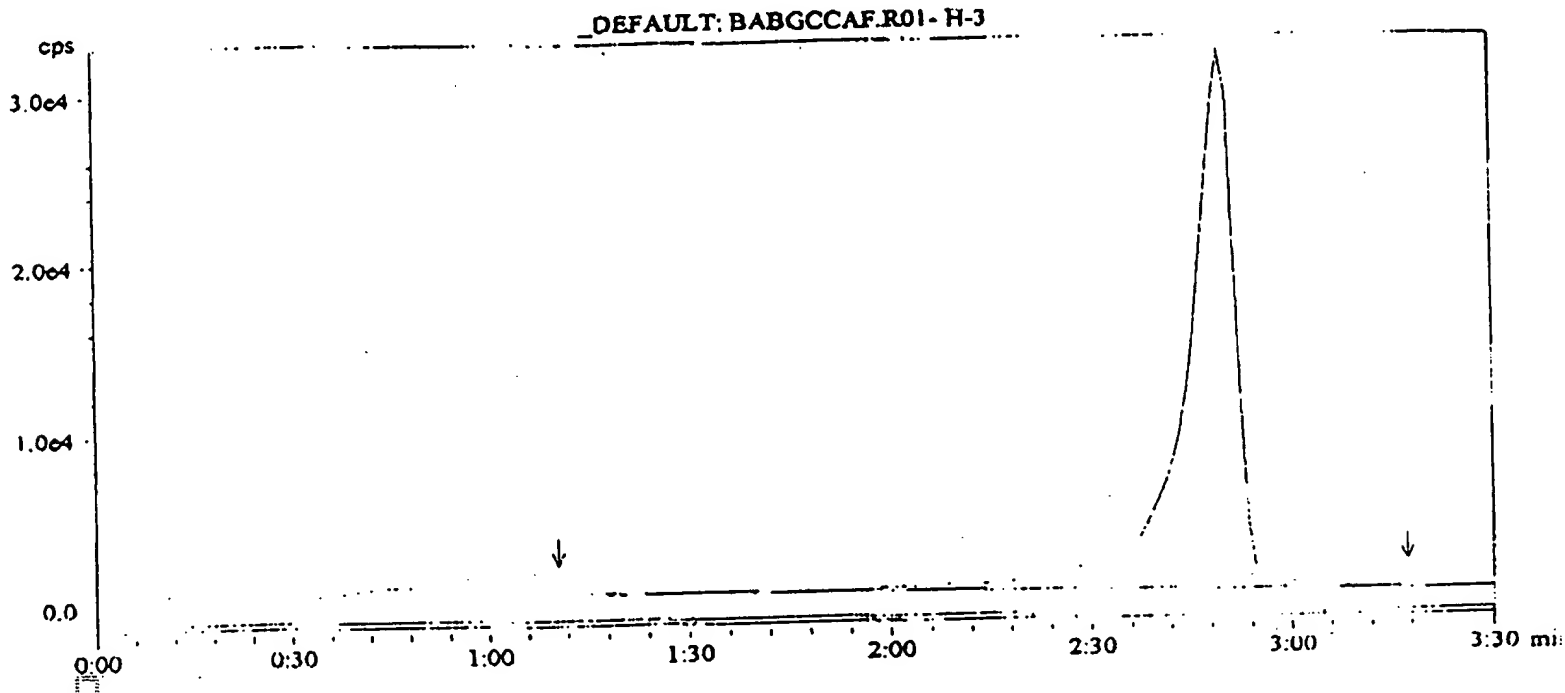


FIG. 62 ^{1}H-NMR of glucosamine.

(^{99m}Tc-[redacted]-DG TLC)



Signals: BABGCCAF.R01

Channel: H-3 Detector:

Name	Start - End		RT	Height (cps)	Area (Counts)	%Total (%)	%ROI (%)
Bkg 1	0: 00-	2: 19	1: 09	539. 7			
Rgn 1	2: 19-	3: 02	2: 47	31606. 2	263570. 8	97. 99	100. 00
Bkg 2	3: 02-	3: 27	3: 14	250. 1			
1 Peak					263570. 8	97. 99	100. 00

Total Area = 268986. 1 Counts
Bkg Area = 89999. 9 Counts
Unallocated = 5415. 3 Counts (2. 01%)

Trace Parameters: BABGCCAF.R01 H-3

Trace Display Smoothing:	0. 0 s
Trace Display Shift:	0. 0 s
Trace Display Factor:	1. 000
Channel Shift:	0. 0 s
Channel Factor:	1. 000

Regions were added manually.

FIG. 63 Radio-TLC analysis of ^{99m}Tc-EC-DG.

^{99m}Tc-EC-deoxyglucose

^{99m}Tc-EC

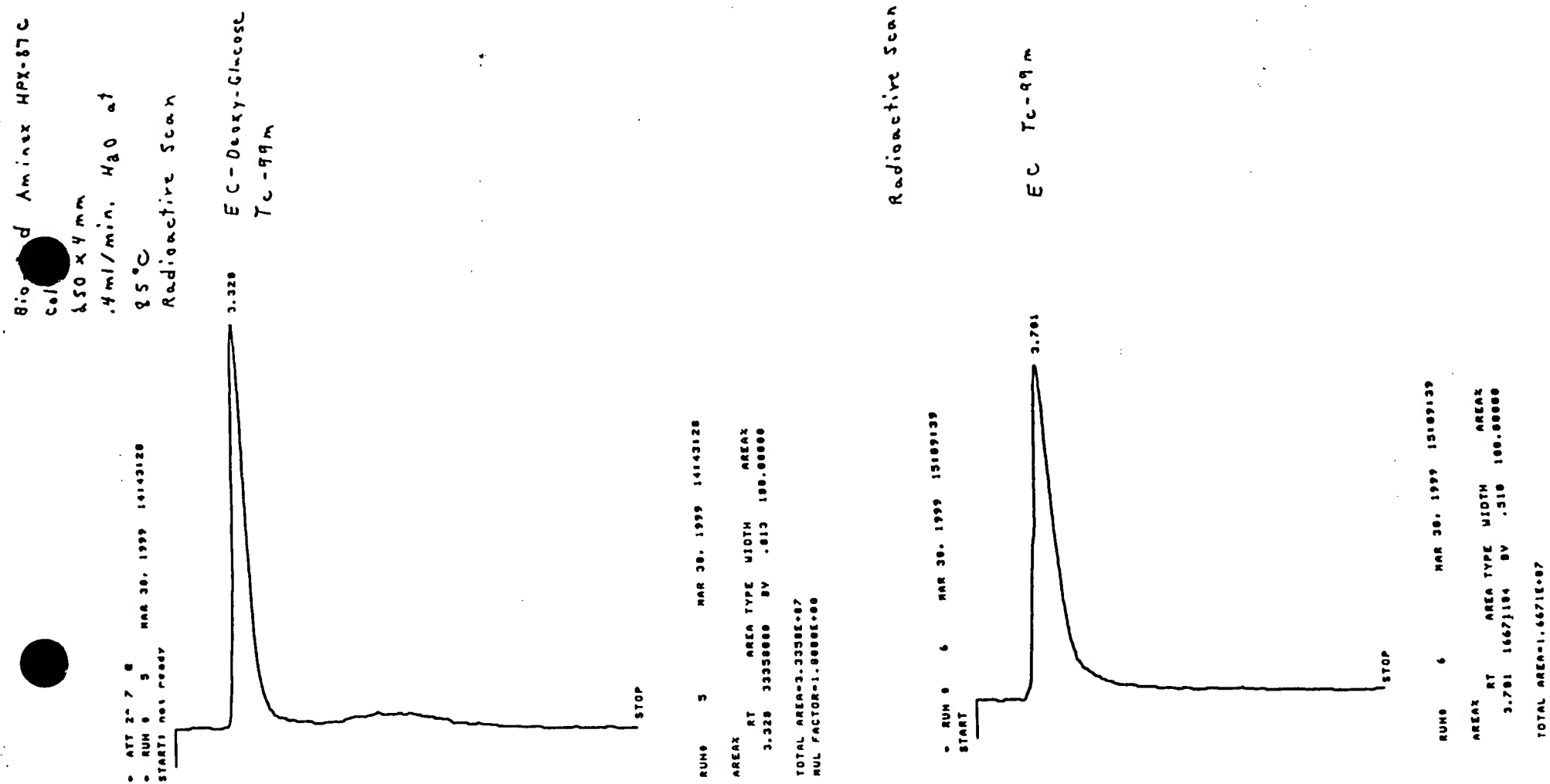


FIG. 64 HPLC analysis of ^{99m}Tc-EC-deoxyglucose and ^{99m}Tc-EC-(radioactive detector).

^{99m}Tc-EC-deoxyglucose + ^{99m}Tc-EC (mixed)

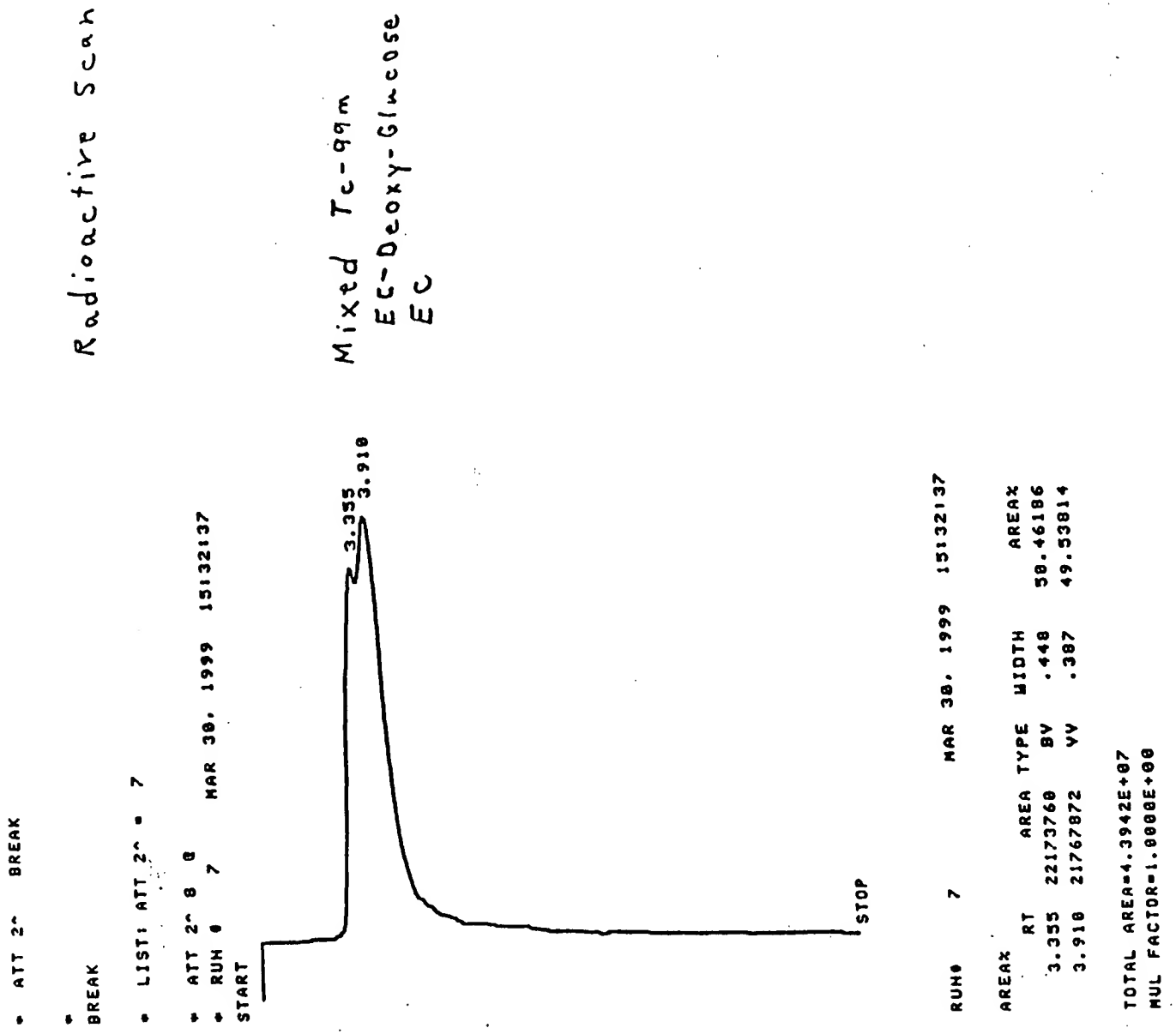


FIG. 65 HPLC analysis of ^{99m}Tc-EC-deoxyglucose and ^{99m}Tc-EC (radioactive detector, mixed).

Hexokinase Assay of Glucose

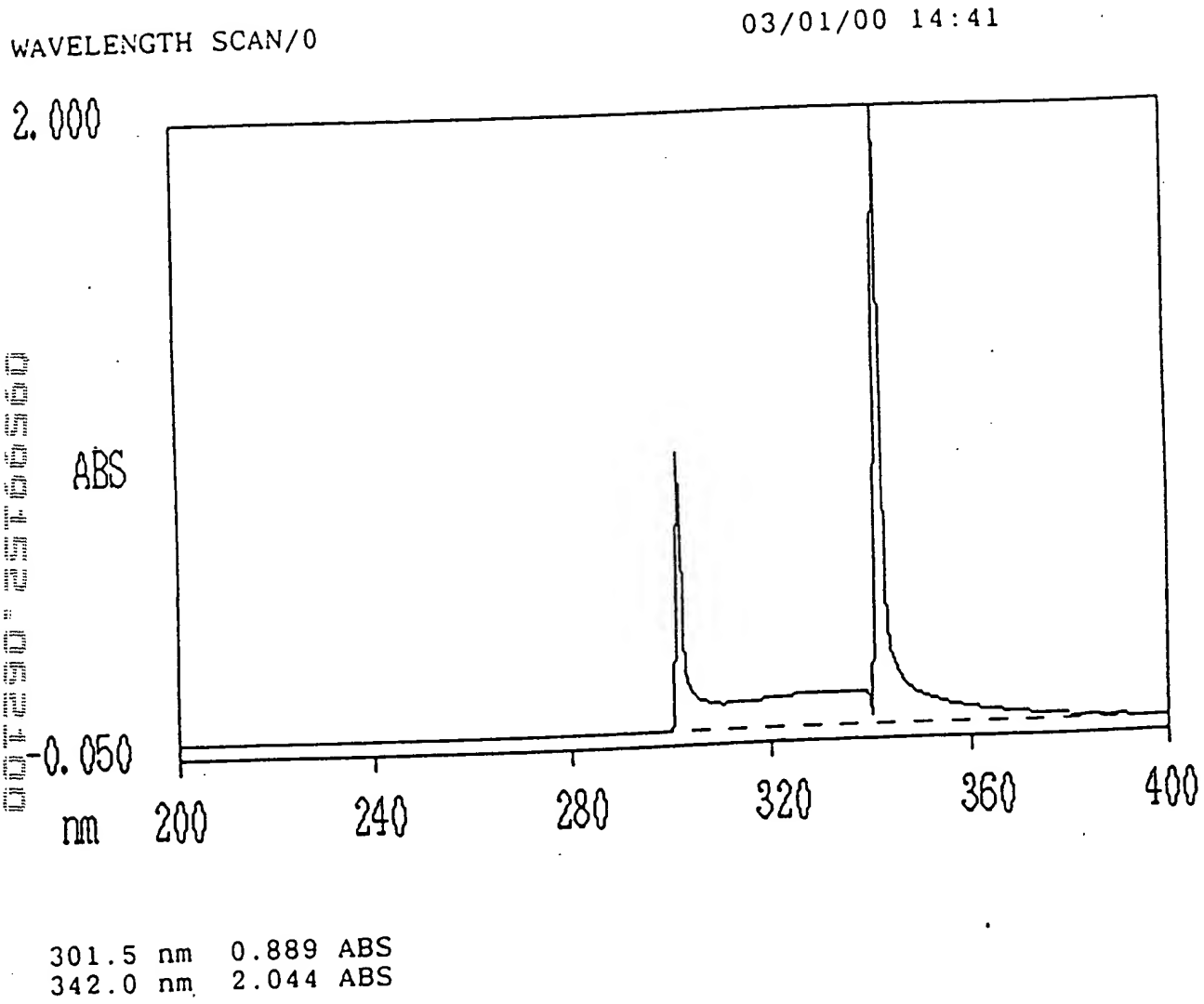


FIG. 66 Hexokinase assay of glucose.

Hexokinase Assay of FDG

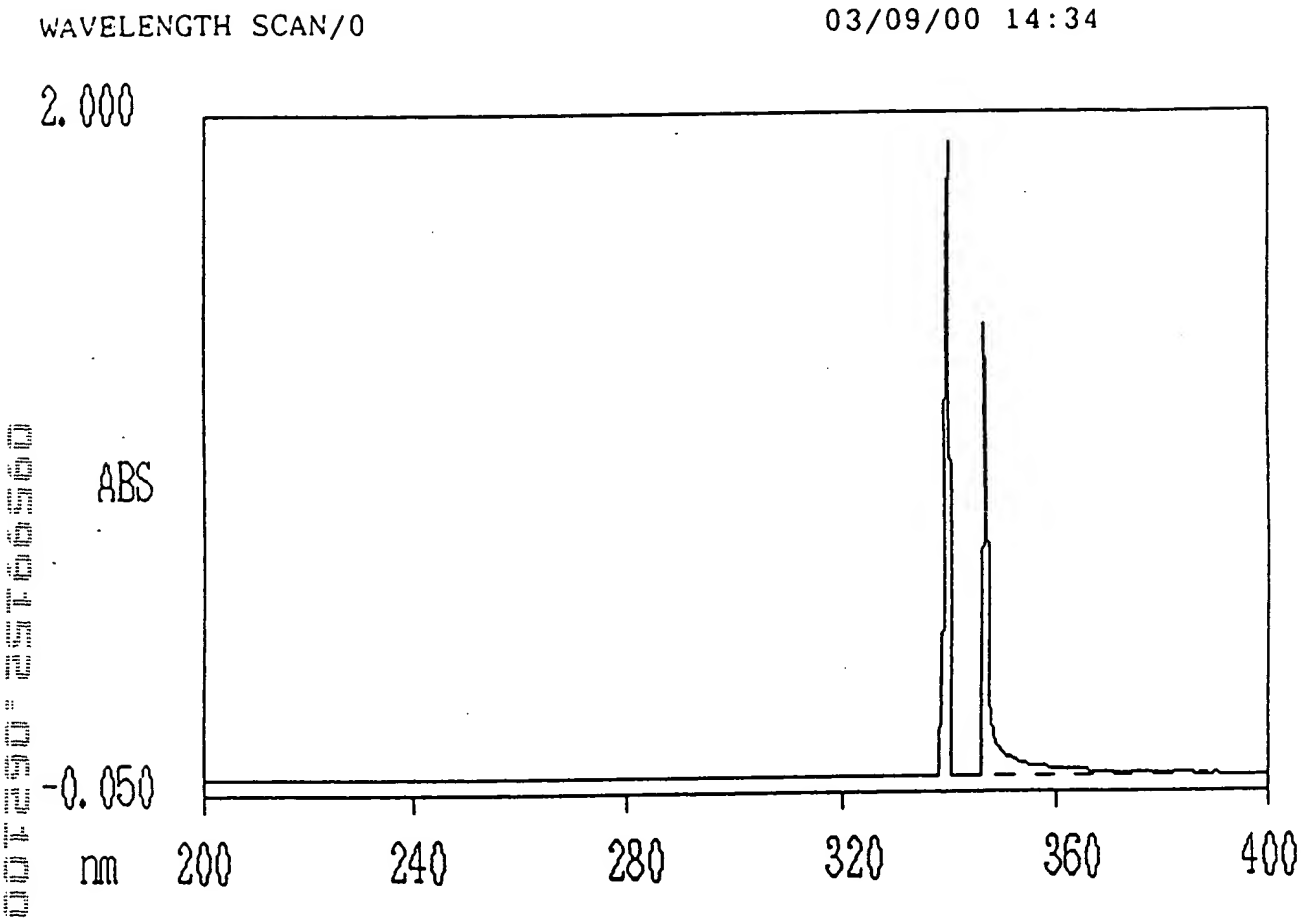


FIG. 67 Hexokinase assay of FDG.

Hexokinase Assay of EC-Glucosamine (EC-DG)

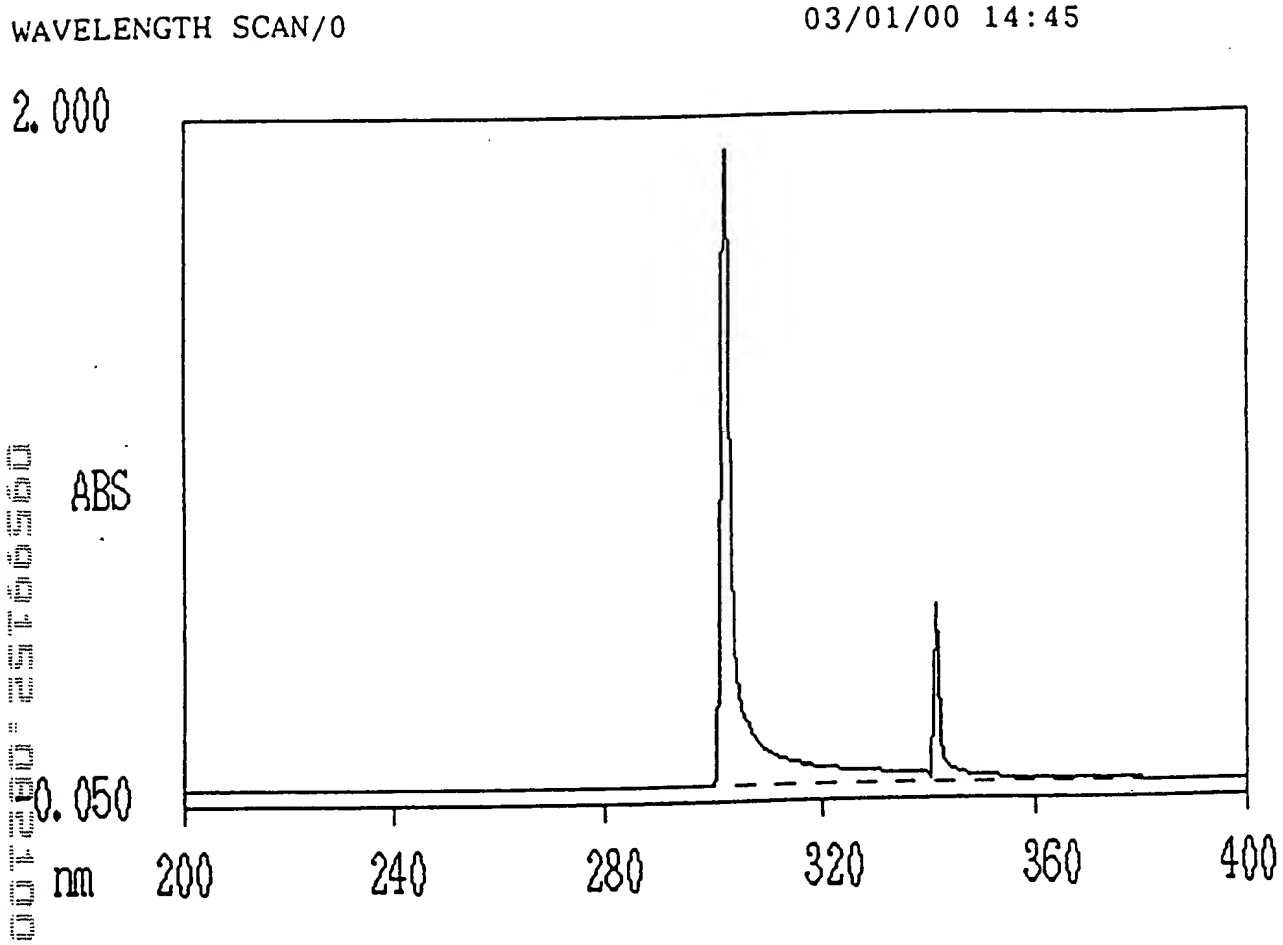


FIG. 68 Hexokinase assay of EC-DG.

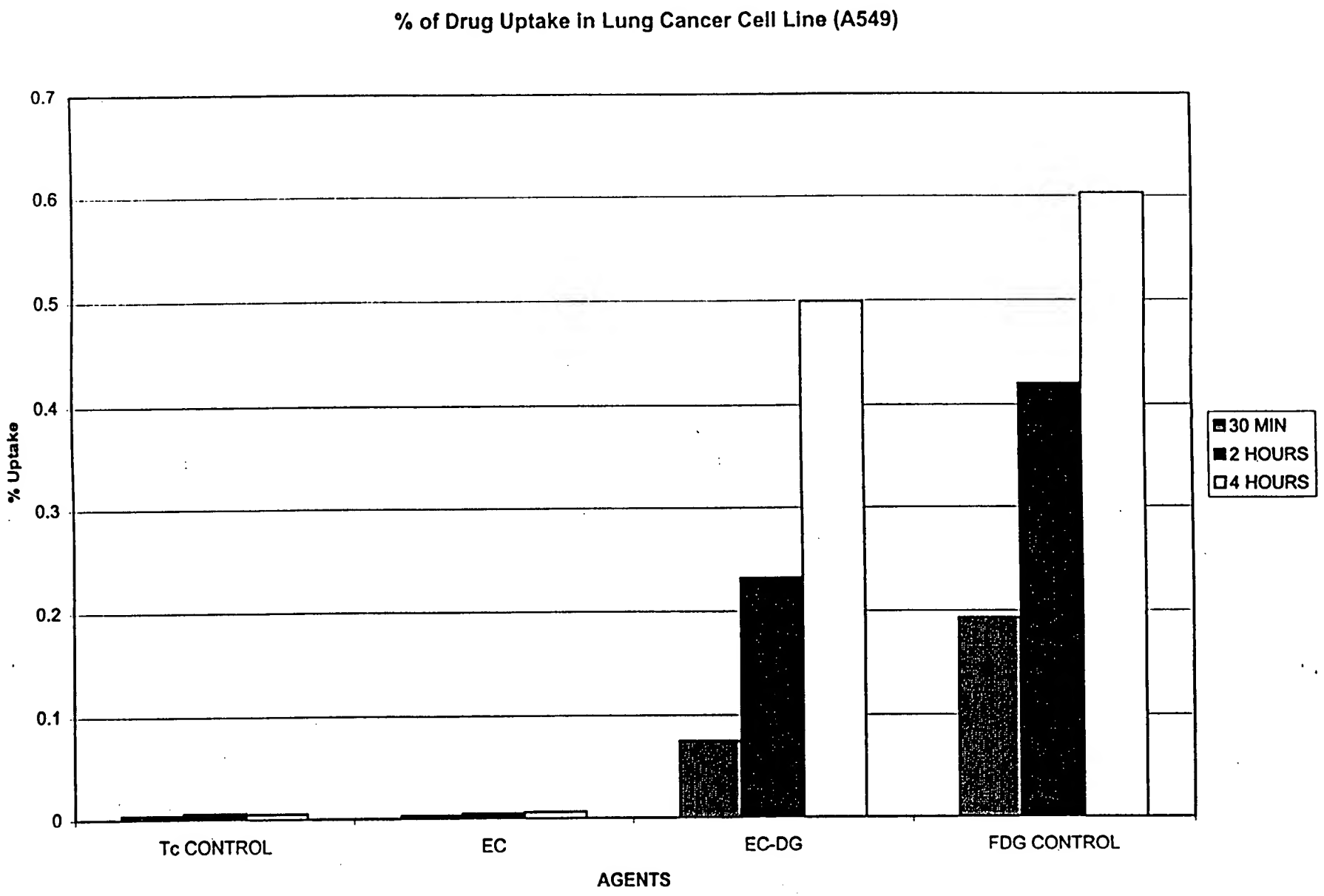


FIG. 69 In vitro cellular uptake assay of ^{99m}Tc-EC-deoxyglucose, ^{99m}Tc-EC and ^{18}F-FDG in lung cancer cell line (A549). ^{99m}Tc-EC-DG showed similar uptake compared to ^{18}F-FDG.

In Vitro Cellular Uptake of ^{99m}Tc-EC-DG in Breast Cancer Cells after Glucose Loading (2 hours incubation; 2uCi/well; 50,000 cells/well; 0.5mL/well)

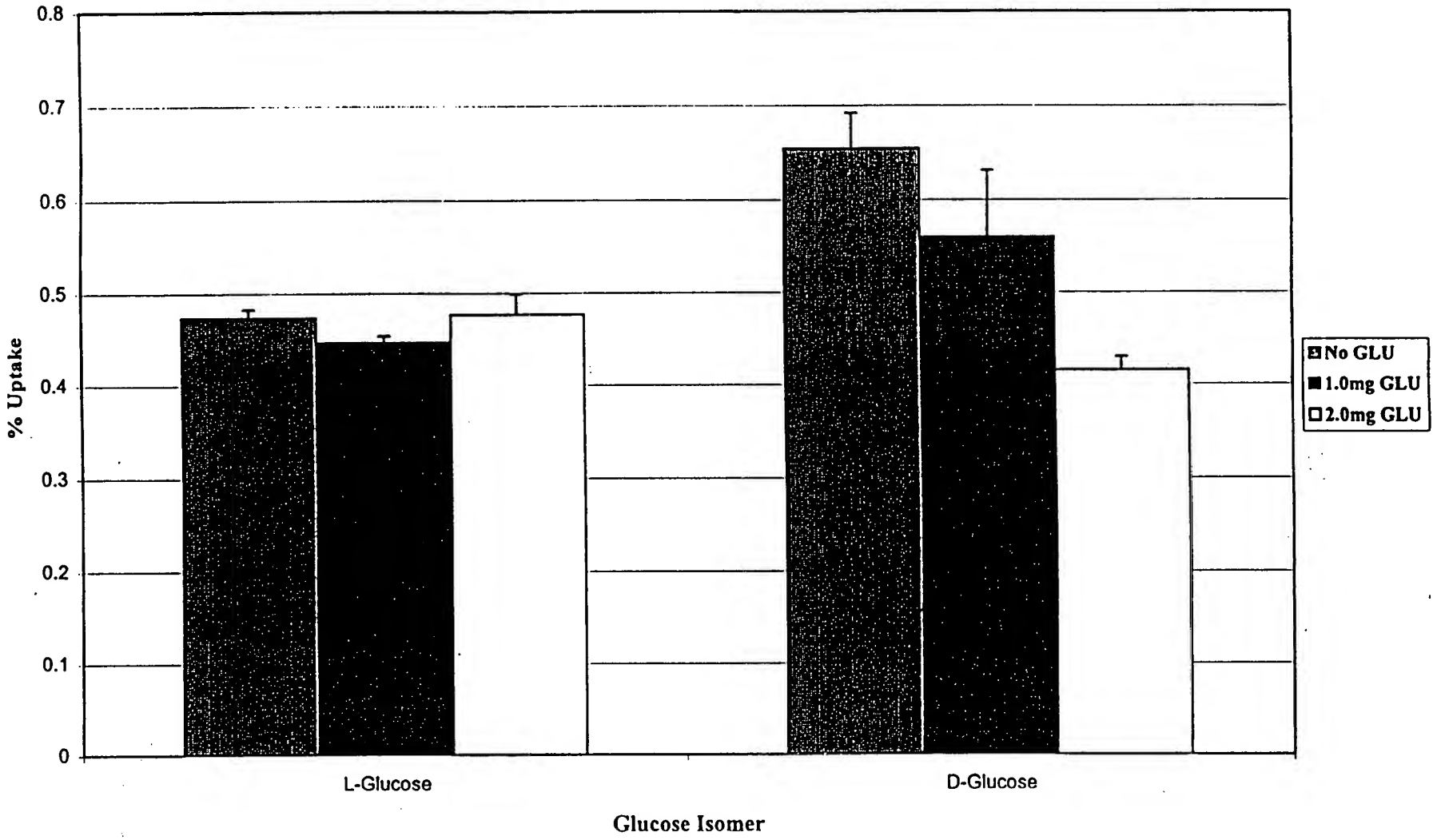


FIG. 70 Effect of d- and l-glucose on breast cellular (13762 cell line) uptake of ^{99m}Tc-EC- DG.

In Vitro Cellular Uptake of ^{18}FDG in Breast Cancer Cells after Glucose Loading (2 hours incubation; 2uCi/well; 50,000 cells/well; 5mL/well)

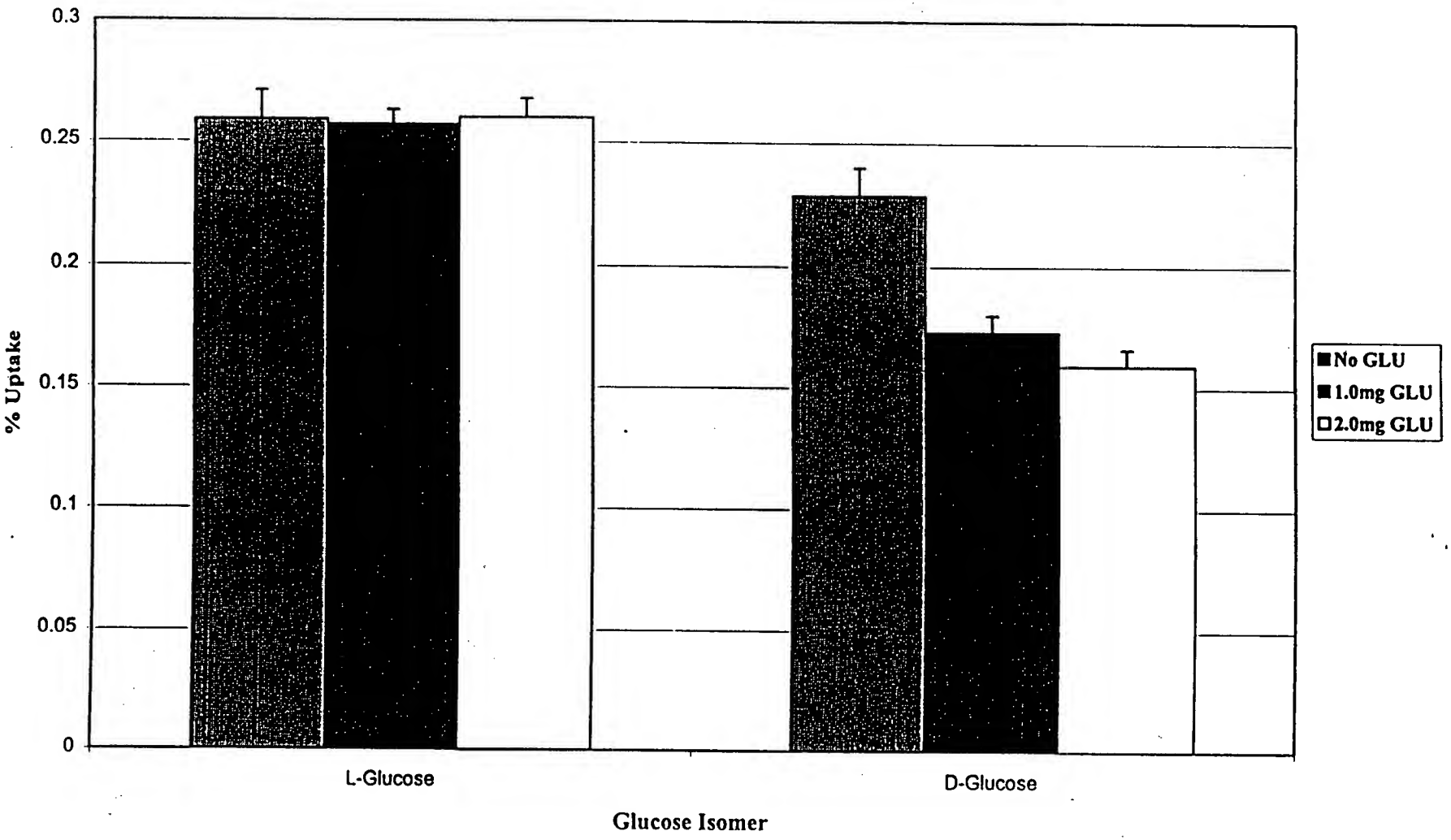


FIG. 71 Effect of d- and l-glucose on breast cellular (13762 cell line) uptake of ^{18}F-FDG.

In Vitro Cellular Uptake of ^{18}FDG in Lung Cancer Cells after Glucose Loading (2 hours incubation; 2uCi/well; 50,000 cells/well; 5mL/well)

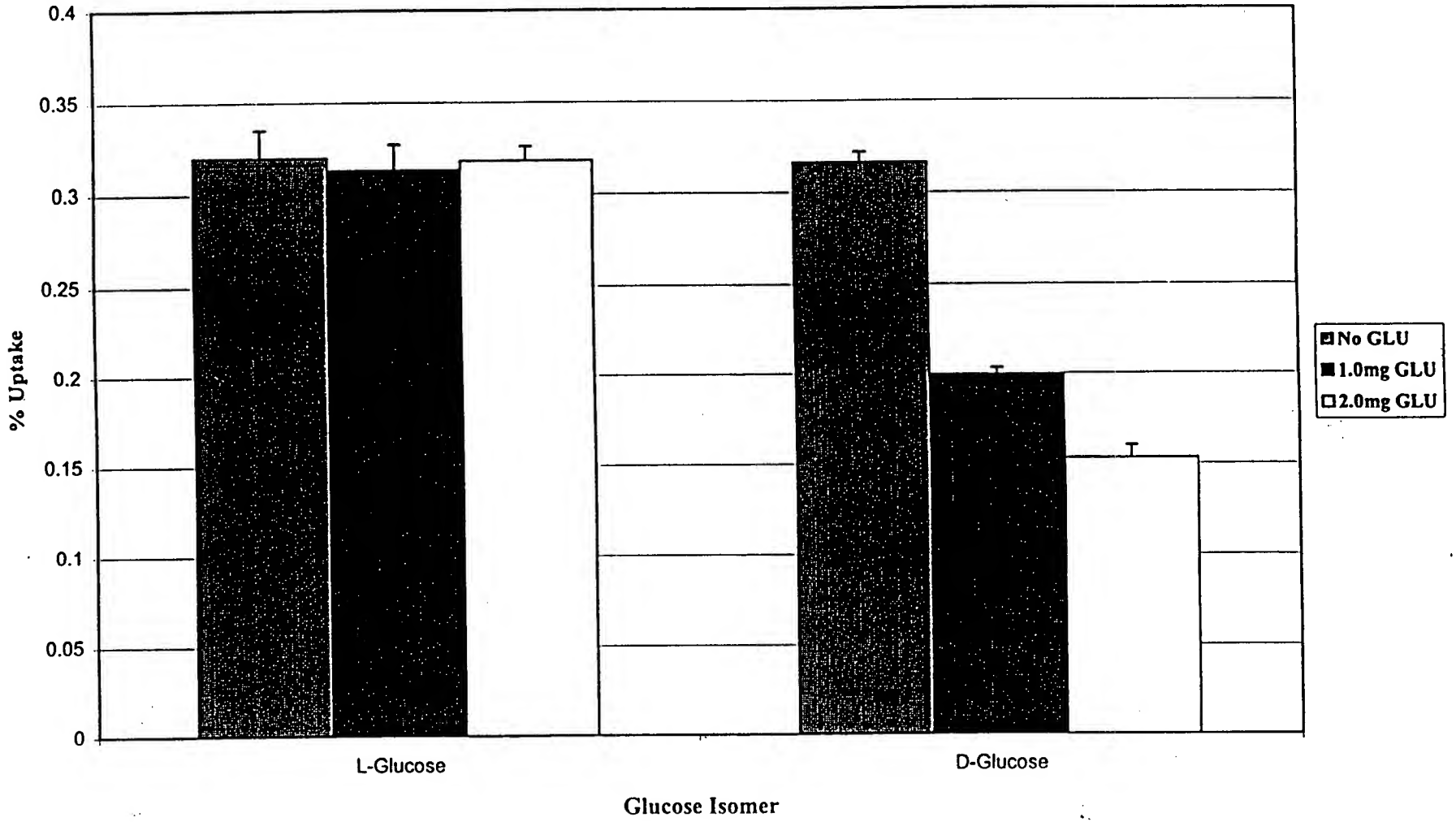


FIG. 72 Effect of d- and l-glucose on lungcellular (A549 cell line) uptake of ^{18}F-FDG.

In Vitro Cellular Uptake of ^{99m}Tc-EC-DG in Lung Cancer Cells after Glucose Loading (2 hours incubation; 2uCi/well; 50,000 cells/well; 0.5mL/well)

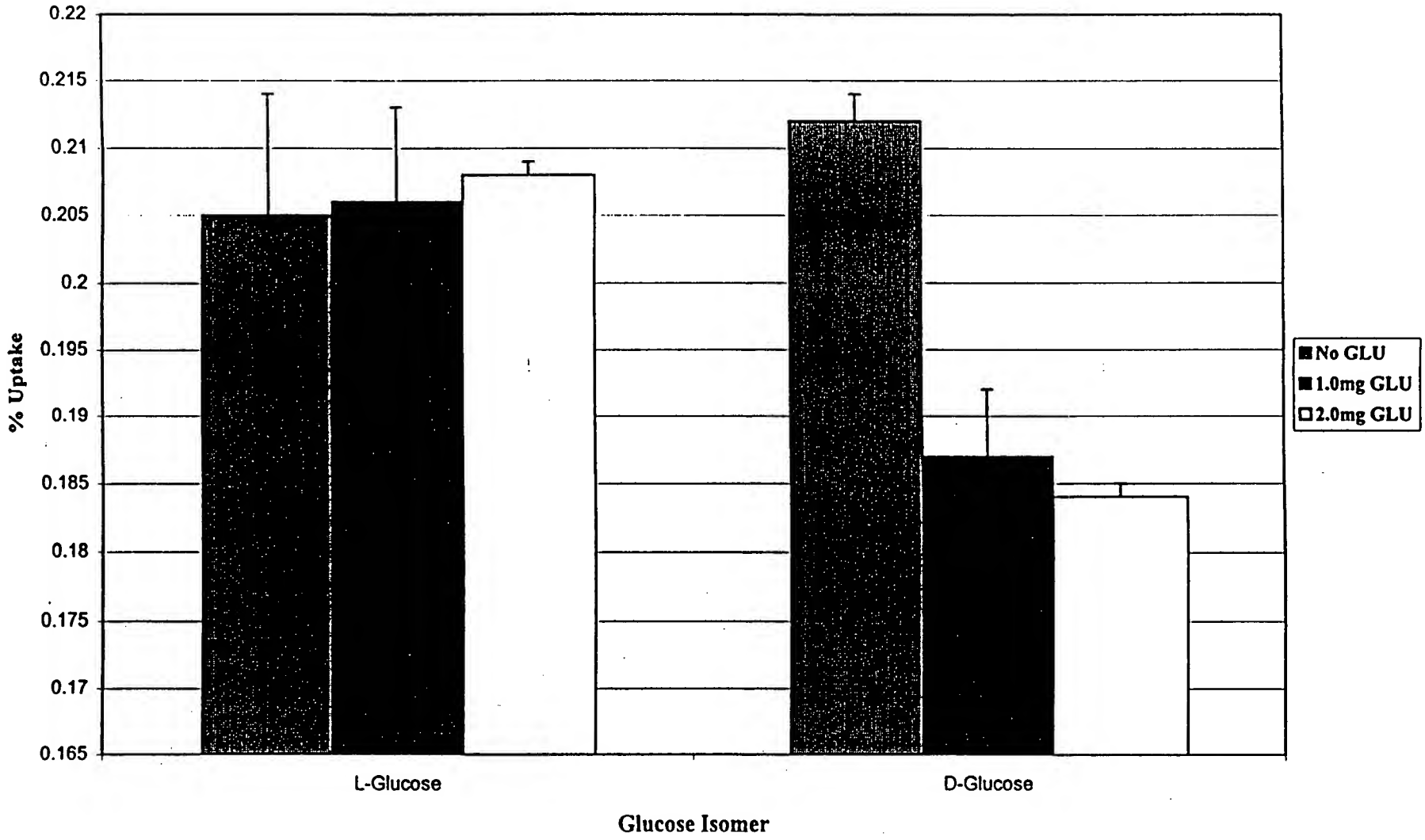


FIG. 73 Effect of d- and l-glucose on breast cellular (A549 cell line) uptake of ^{99m}Tc-EC- DG.

Effect of Intravenous Injection of Glucosamine and EC-DG on Blood Glucose Level in Rats

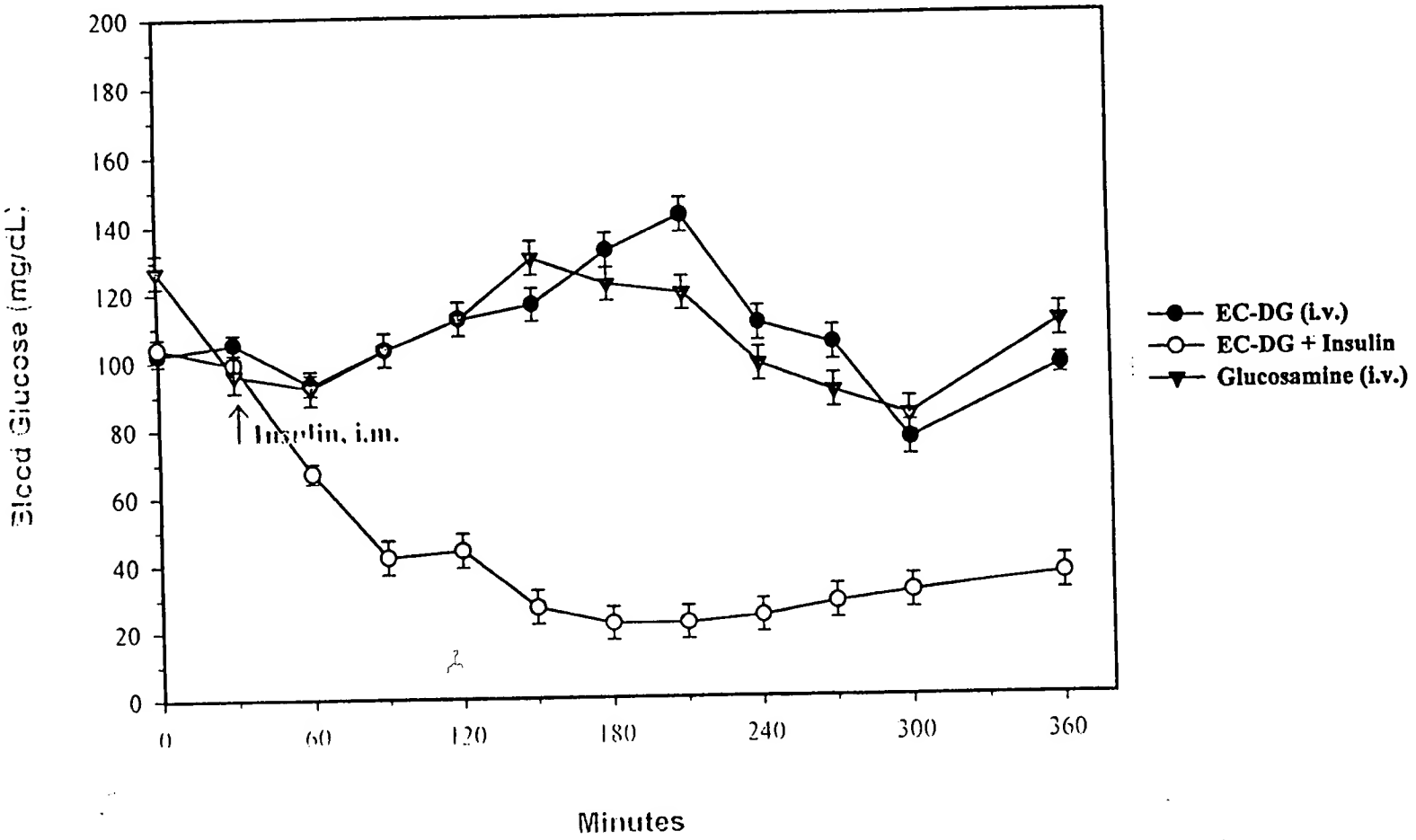


FIG. 74 Effect of *in vivo* blood glucose level induced by glucosamine and EC-DG (1.2 mmol/kg, i.v.).

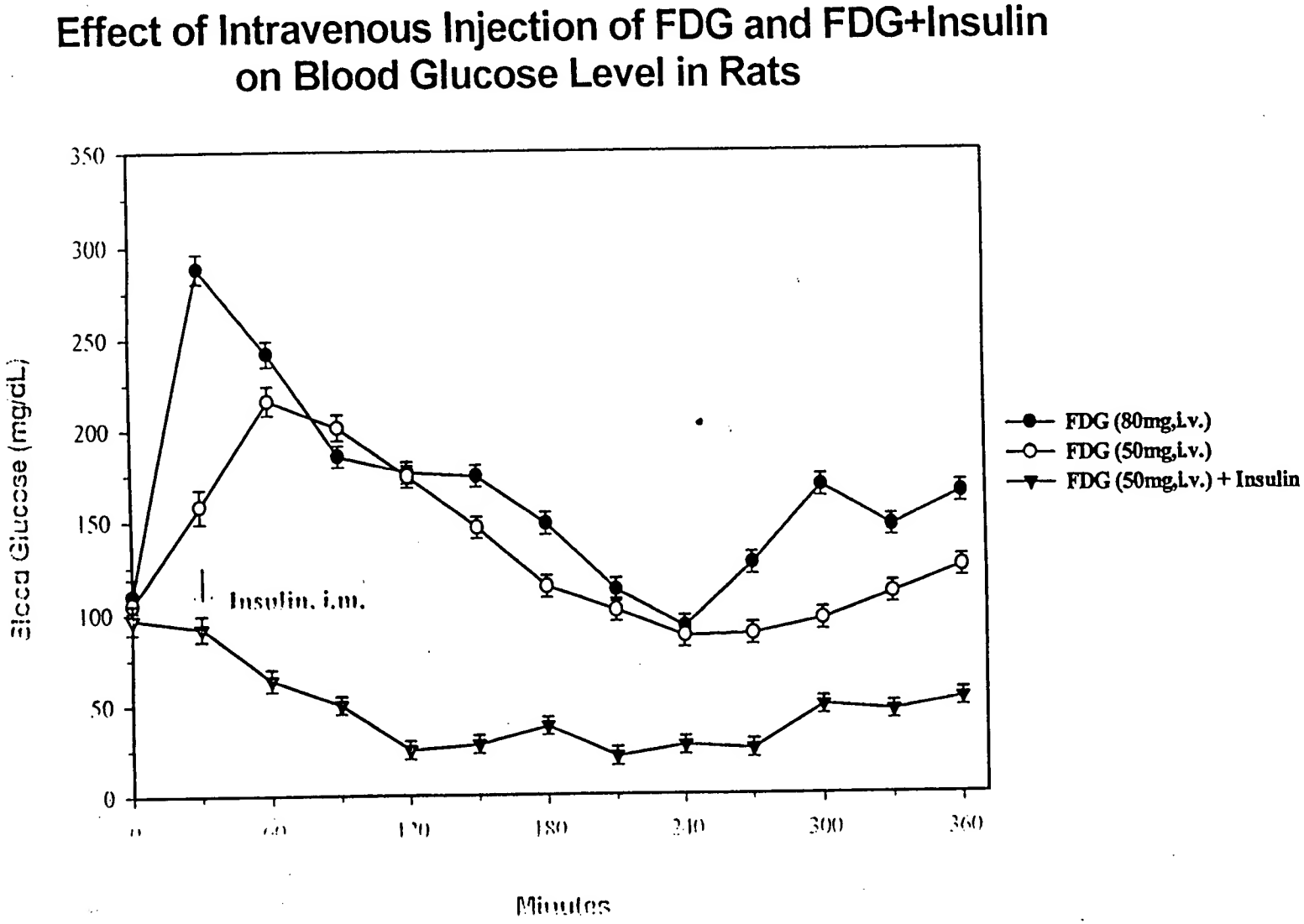


FIG. 75 Effect of *in vivo* blood glucose level induced by FDG (1.2 and 1.9 mmol/kg, i.v.)and insulin.

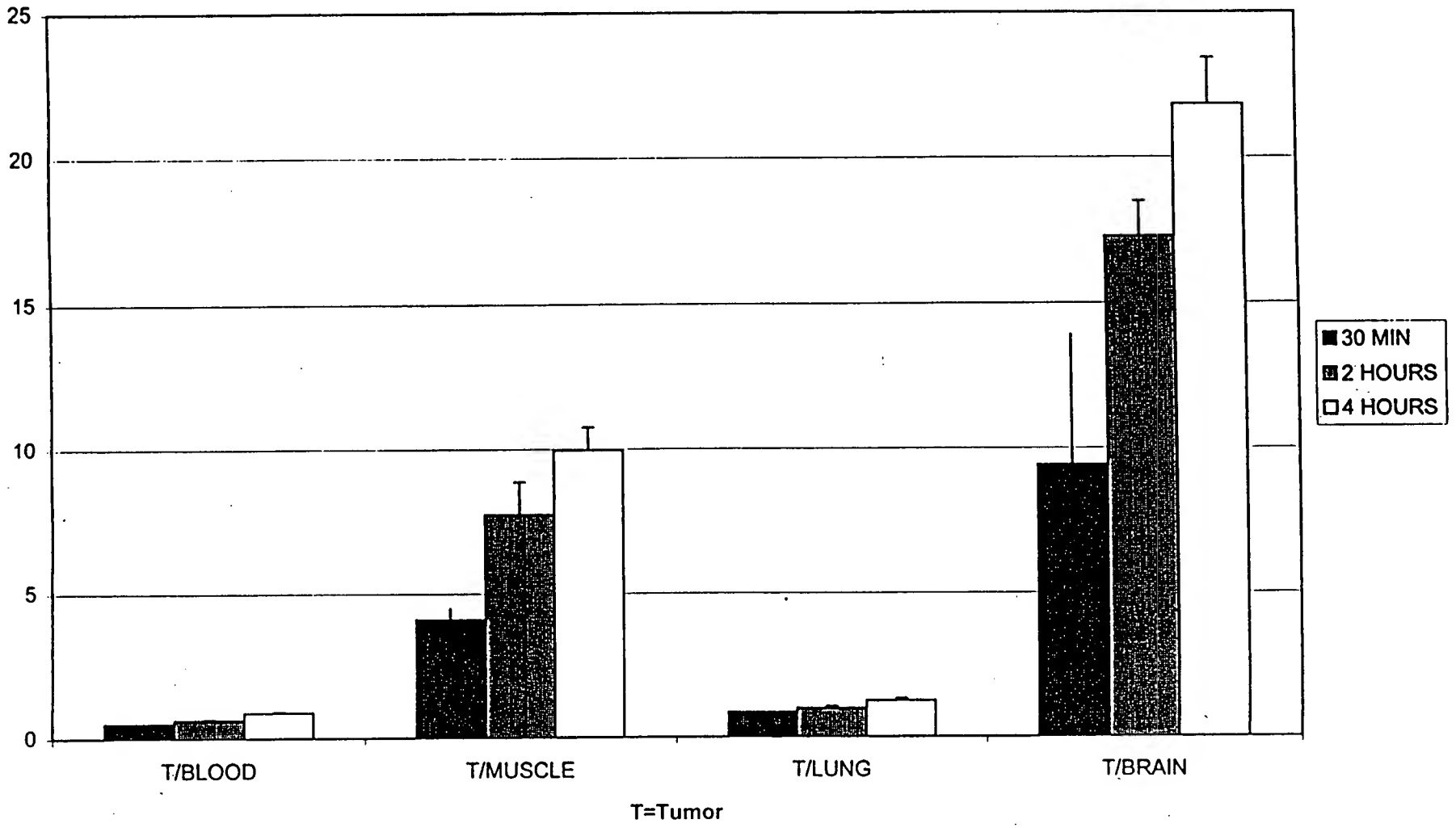


FIG. 76 Tumor-to-tissue count density ratios of ^{99m}Tc-EC-deoxyglucose in breast tumor-bearing rats.

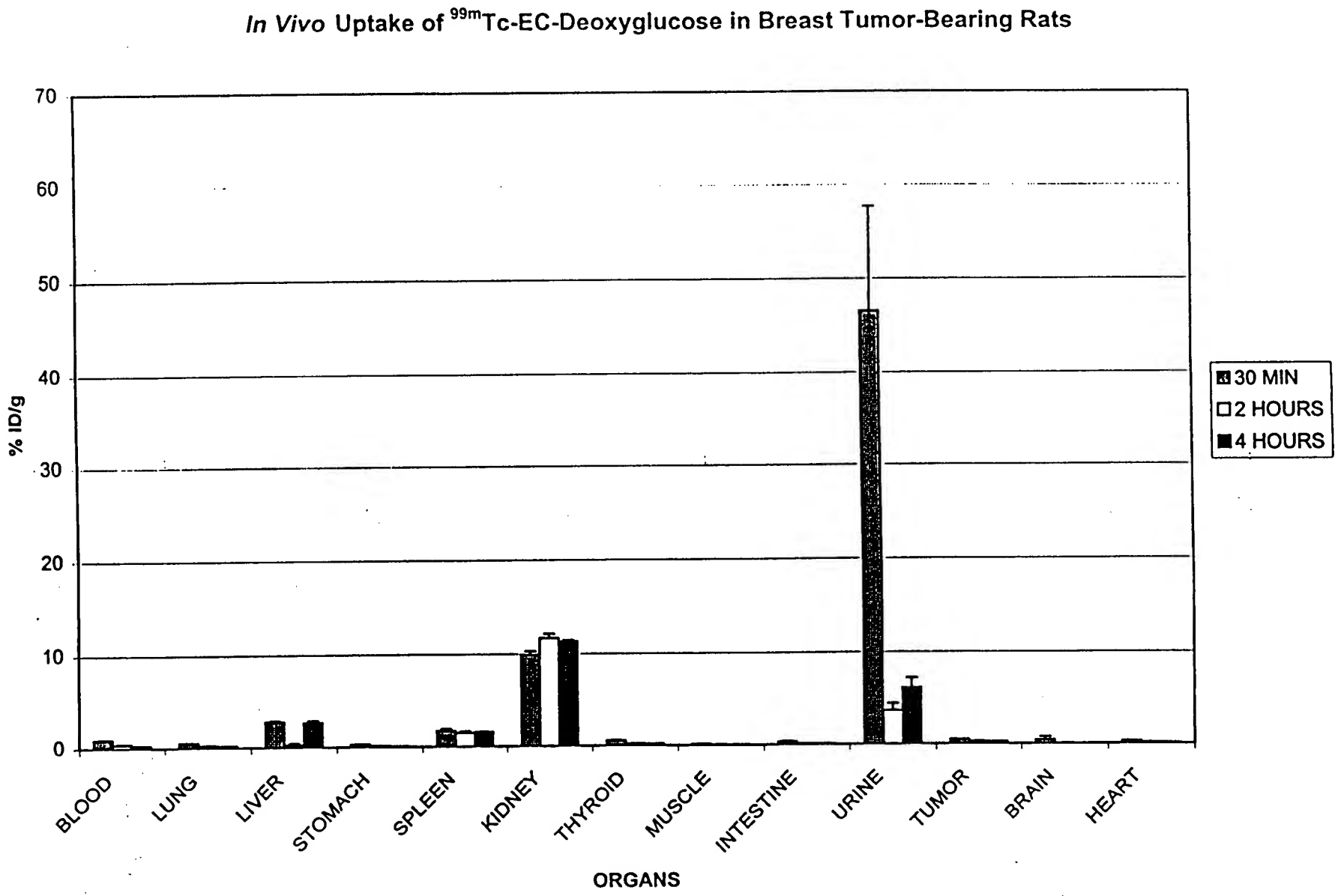


FIG. 77 In vivo biodistribution of ^{99m}Tc-EC-deoxyglucose in breast tumor-bearing rats.

In Vivo Uptake of ^{99m}Tc-EC-Deoxyglucose in Lung Tumor-Bearing Nude Mice

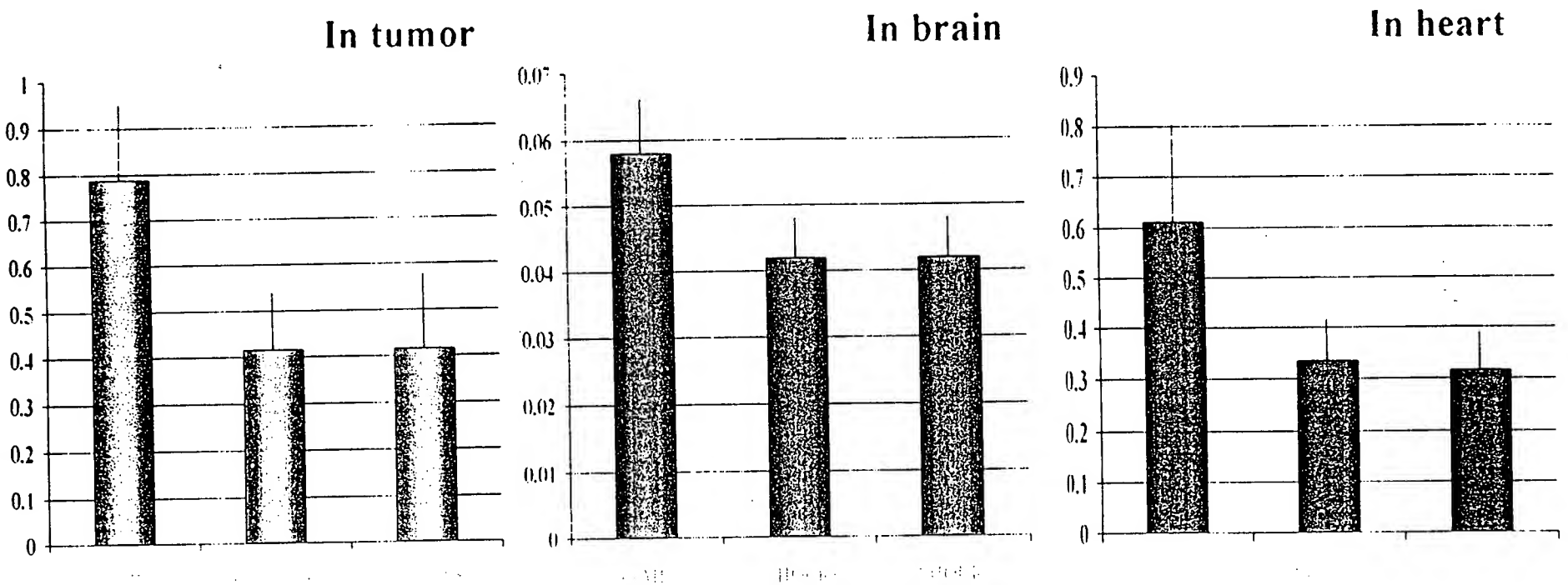


FIG. 78 In vivo tissue uptake of ^{99m}Tc-EC-deoxyglucose in lung tumor-bearing mice.

In Vivo Uptake of ^{99m}Tc-EC-Neomycin in Lung Tumor-Bearing Nude Mice

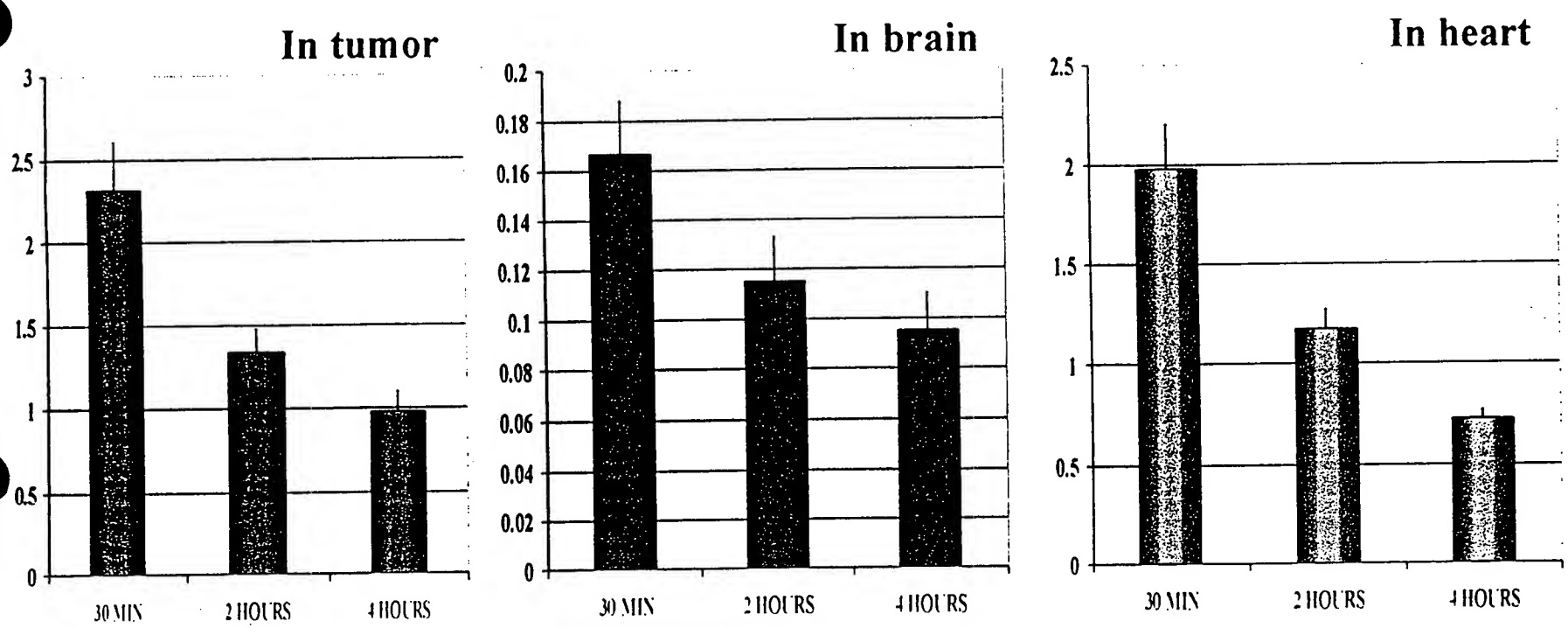


FIG. 79 In vivo tissue uptake of ^{99m}Tc-EC-neomycin in lung tumor-bearing mice.

In Vivo Uptake of ^{18}FDG in Lung Tumor-Bearing Nude Mice

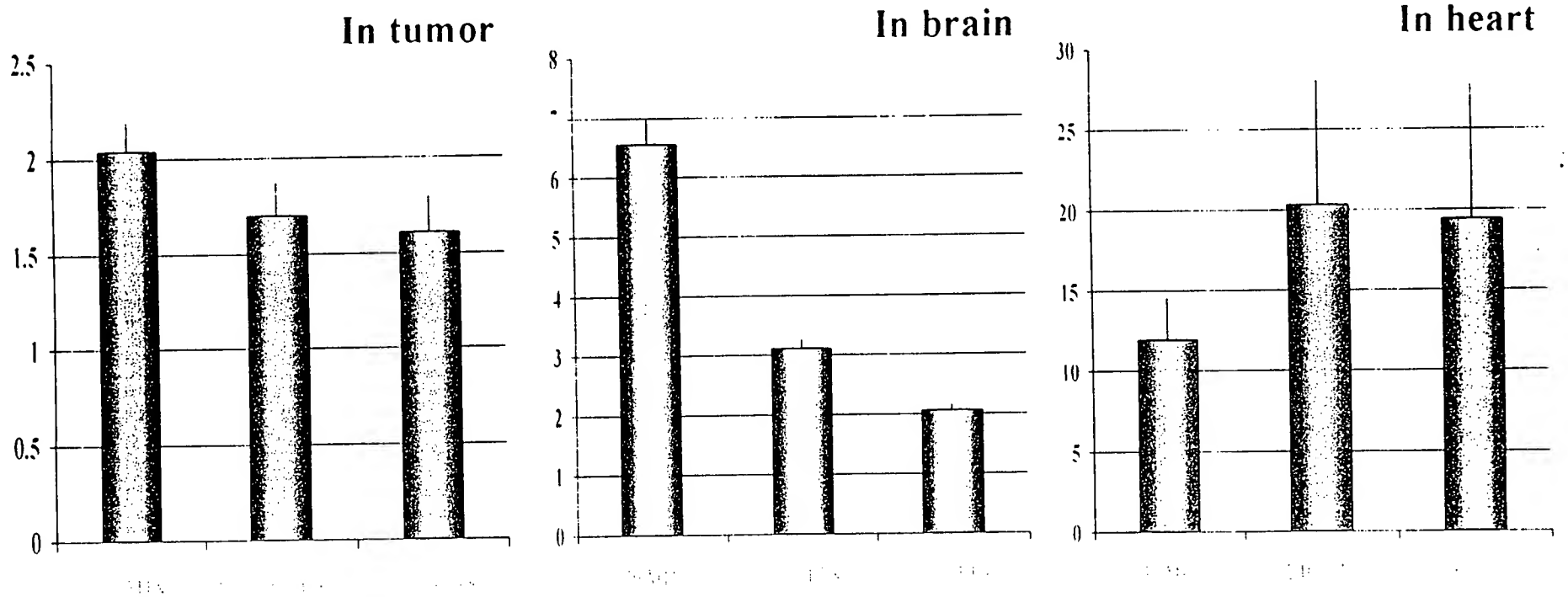
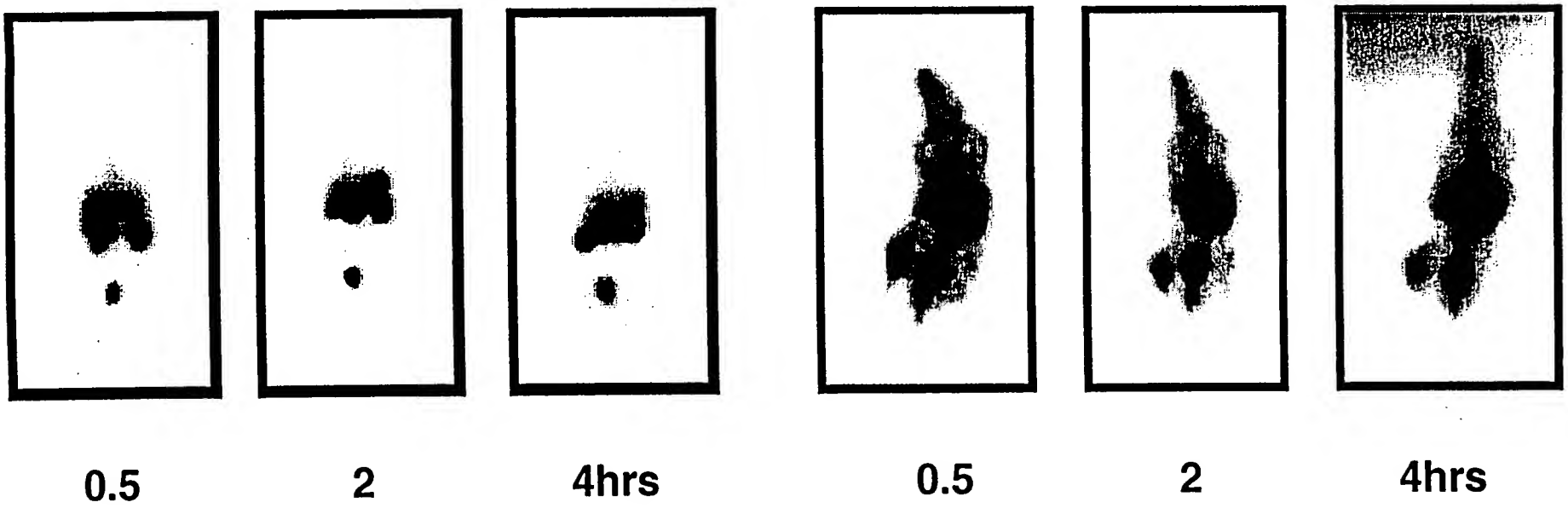


FIG. 80 In vivo tissue uptake of ^{18}F-FDG in lung tumor-bearing mice.

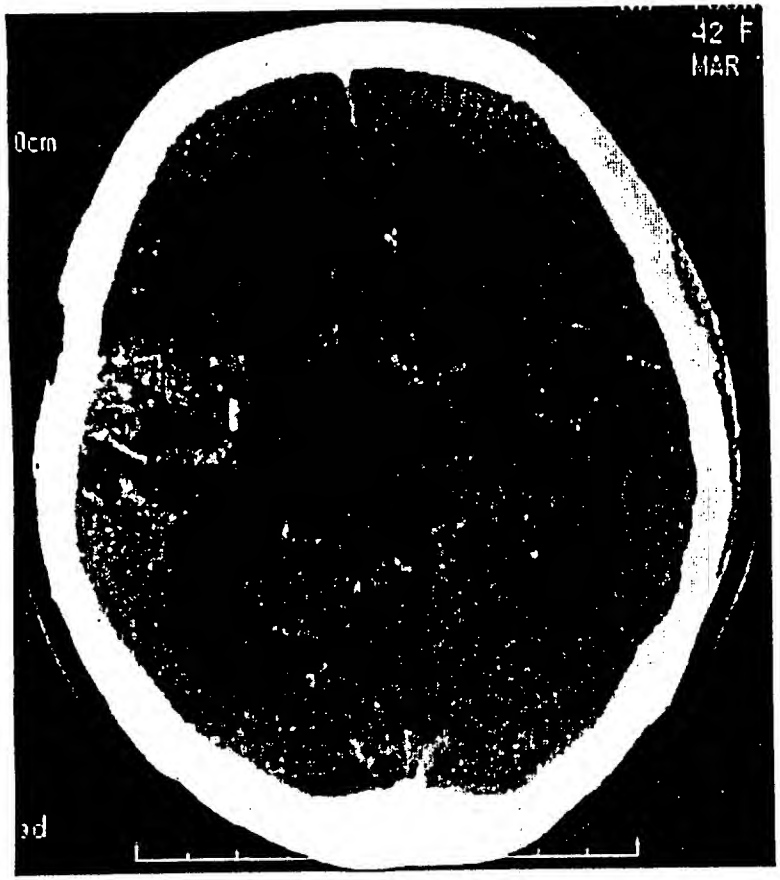


Planar image of breast tumor-bearing rats after administration of ^{99m}Tc-EC and ^{99m}Tc-EC-Glucose(6) (100μCi/rat, iv.) showed that the tumor could be well visualized from 0.5-4 hours postinjection.

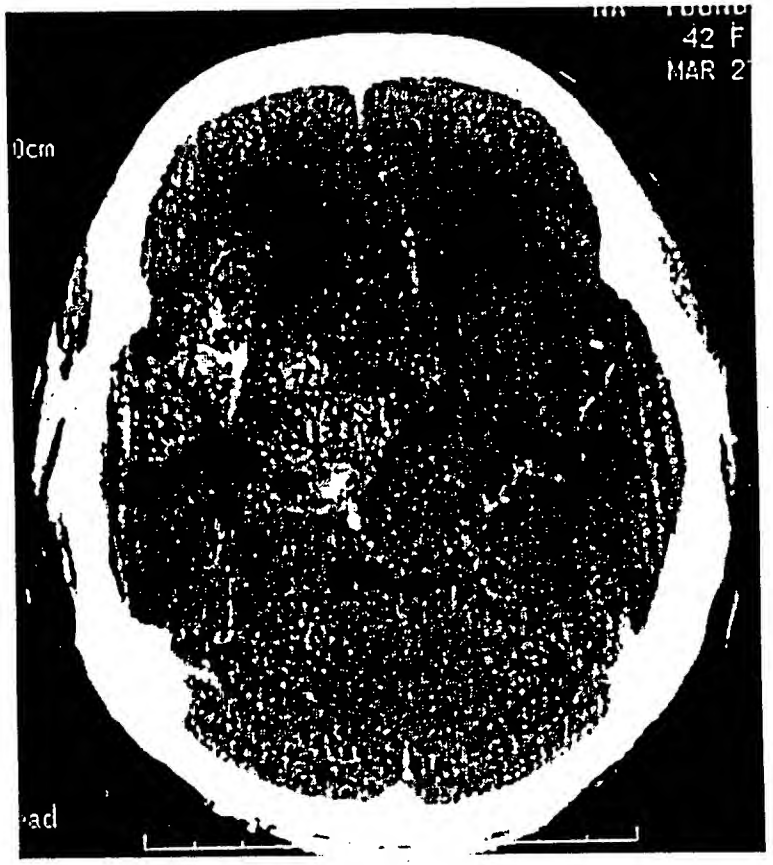
FIG. 81 Planar image of breast tumor-bearing rats after admiinistaration of ^{99m}Tc-EC and ^{99m}Tc-EC-deoxyglucose (100 μCi/rat, iv.) showed that the tumor could be well visualized from 0.5-4 hous

Case 1 1/42

Dx : anaplastic astrocyloma



Pre OP



Post OP

FIG. 82A MRI of a patient with astrocytoma.

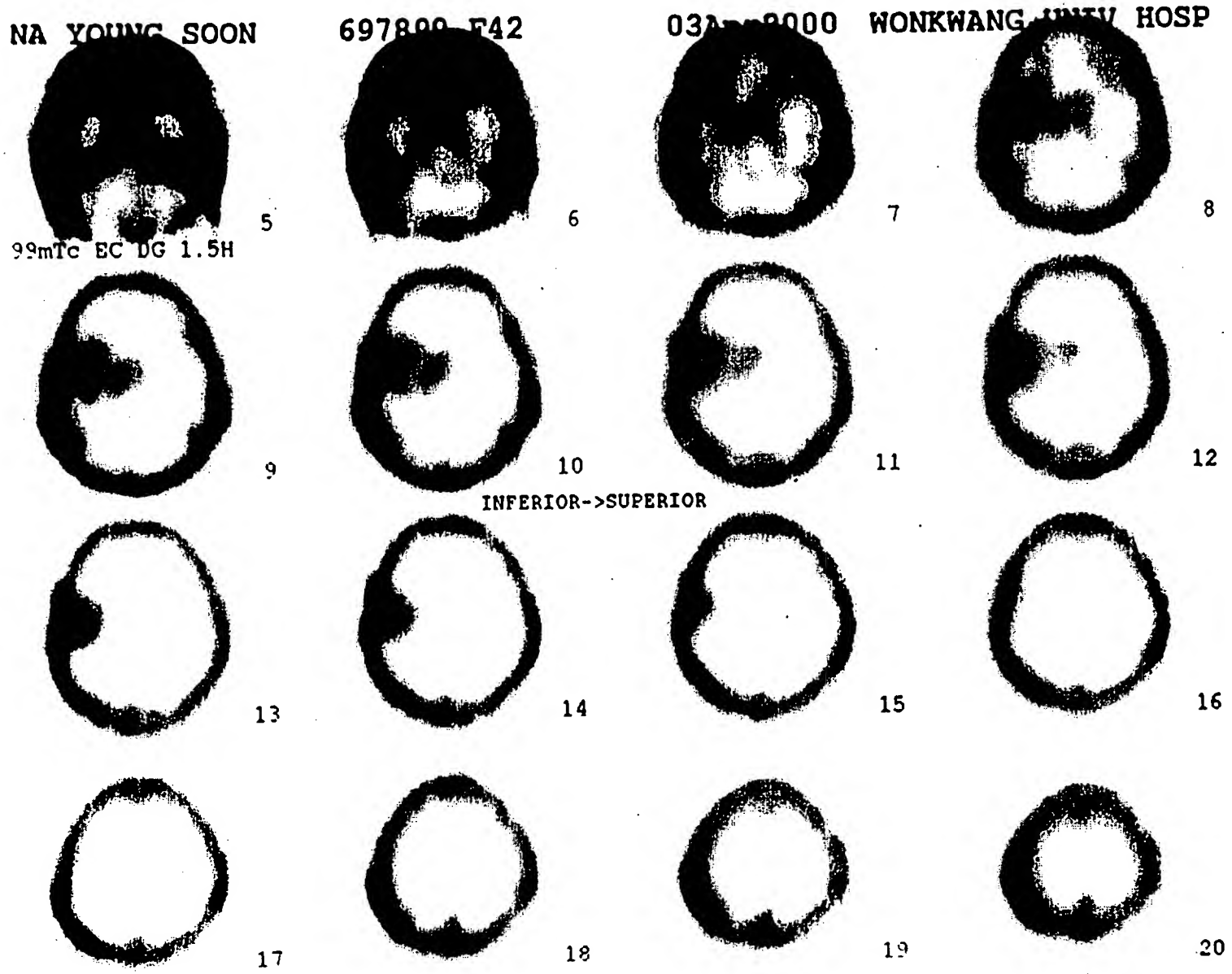
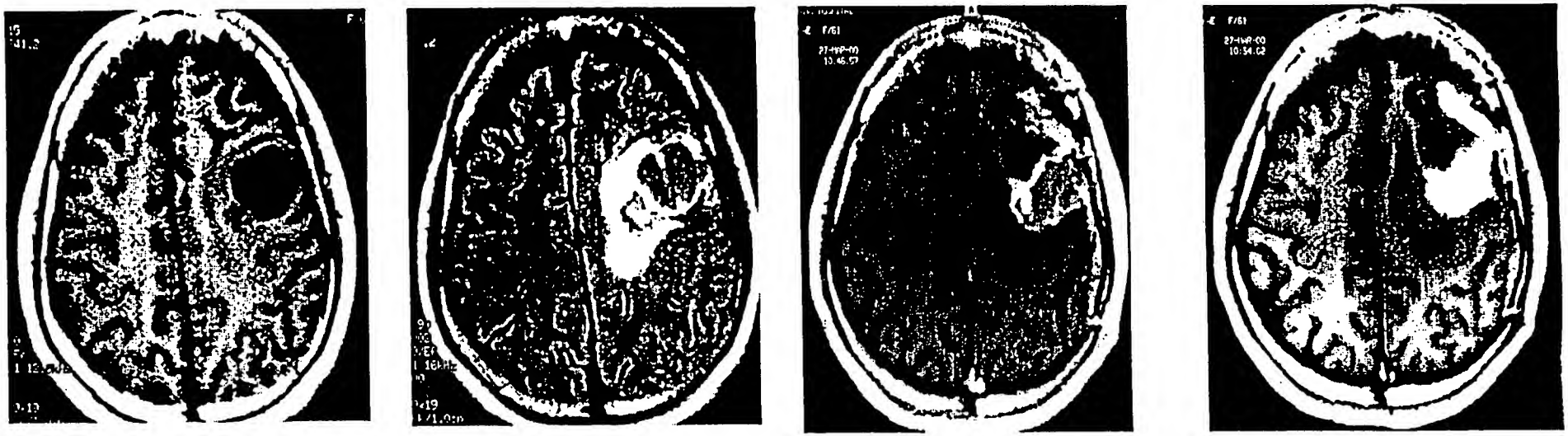


FIG. 82B SPECT with ^{99m}Tc-EC-DG of a patient with astrocytoma.

Case [illegible] F/61

Dx: anaplastic astrocytoma with hemorrhage



Pre –OP

Post–OP

FIG. 83A MRI of a patient with hemorrhagic astrocytoma.

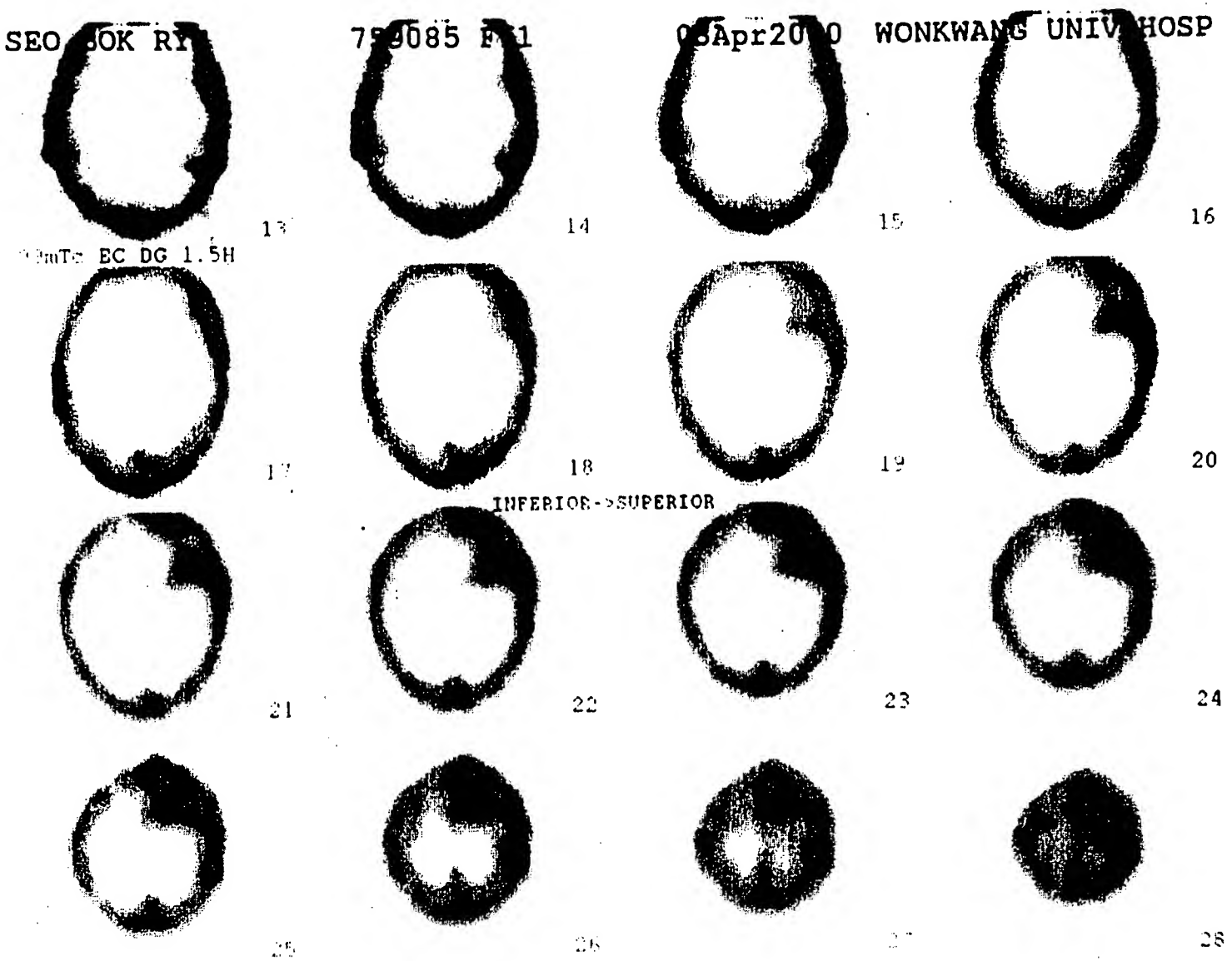


FIG. 83B SPECT with ^{99m}Tc-EC-DG of a patient with astrocytoma.

Case 5 : M/62

Dx : Meningioma

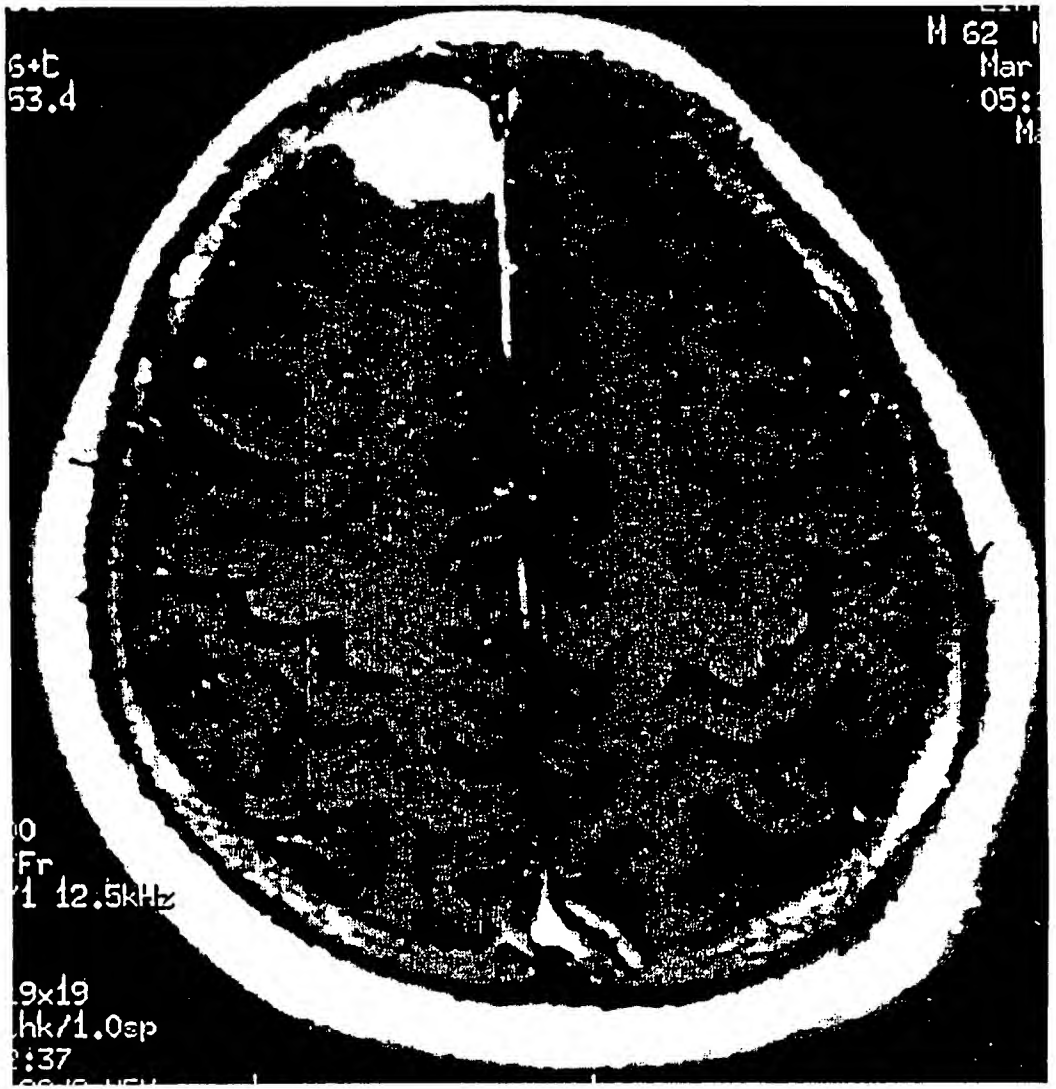


FIG. 84A MRI of a patient with benign meningioma.

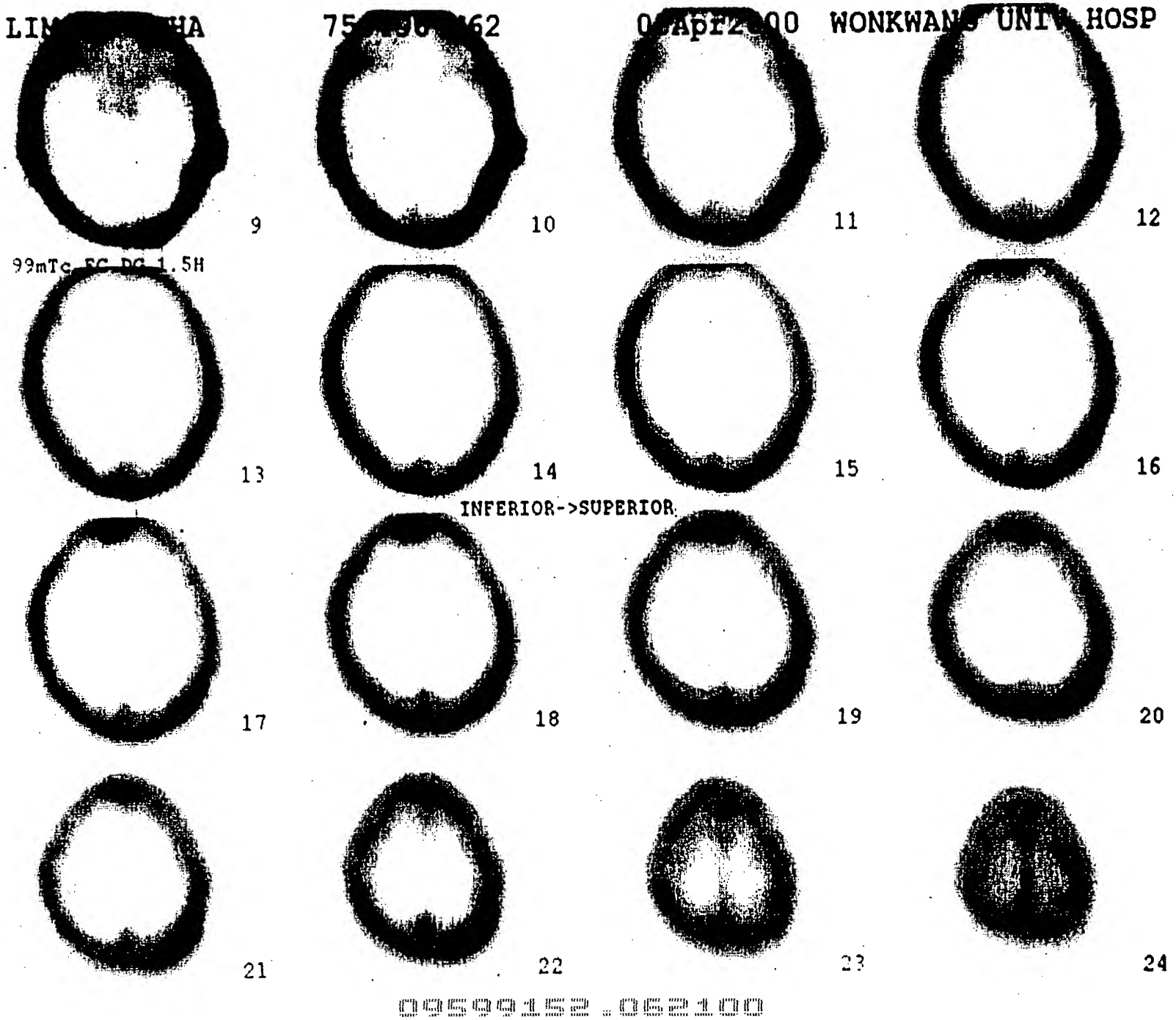
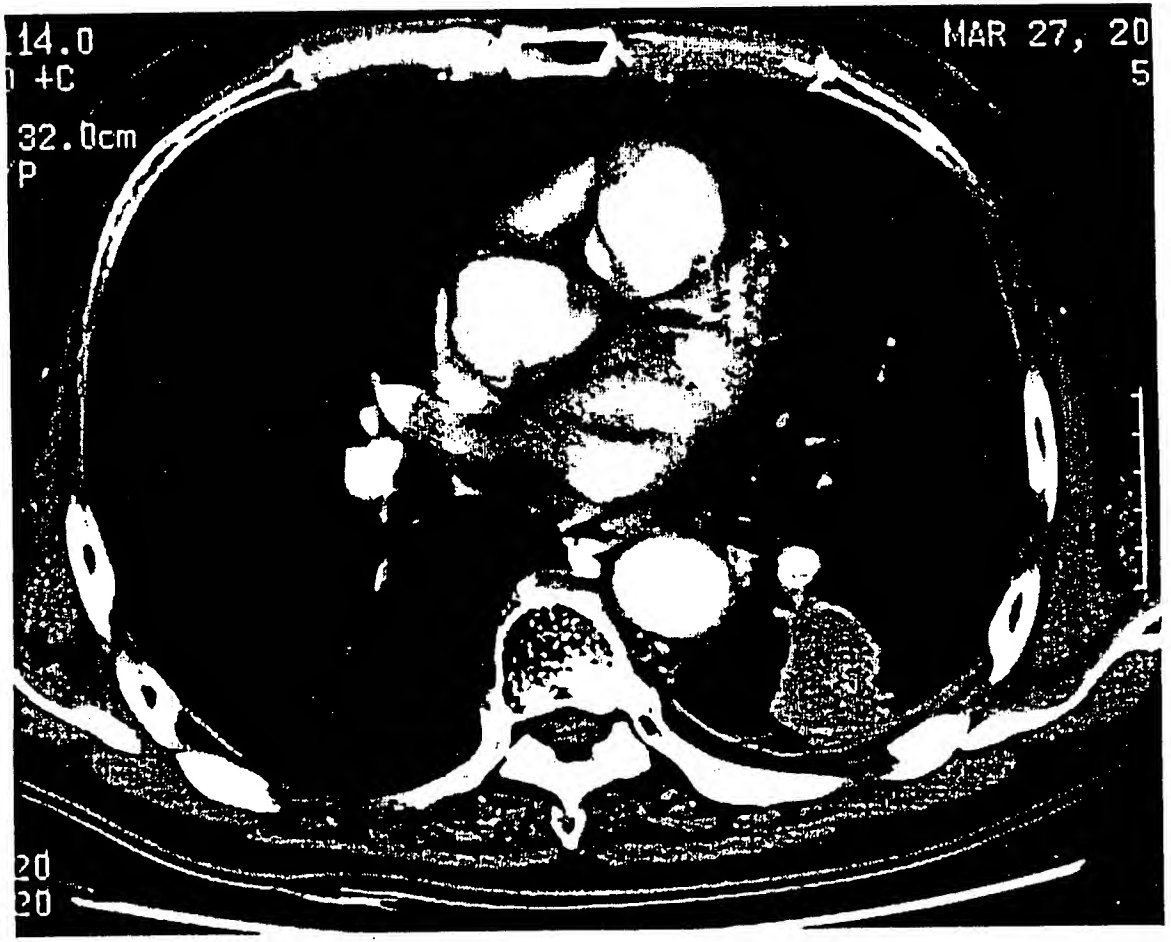


FIG. 84B SPECT with ^{99m}Tc-EC-DG of a patient with benign meningioma showed no focal intensed uptake

Case 1. M/C

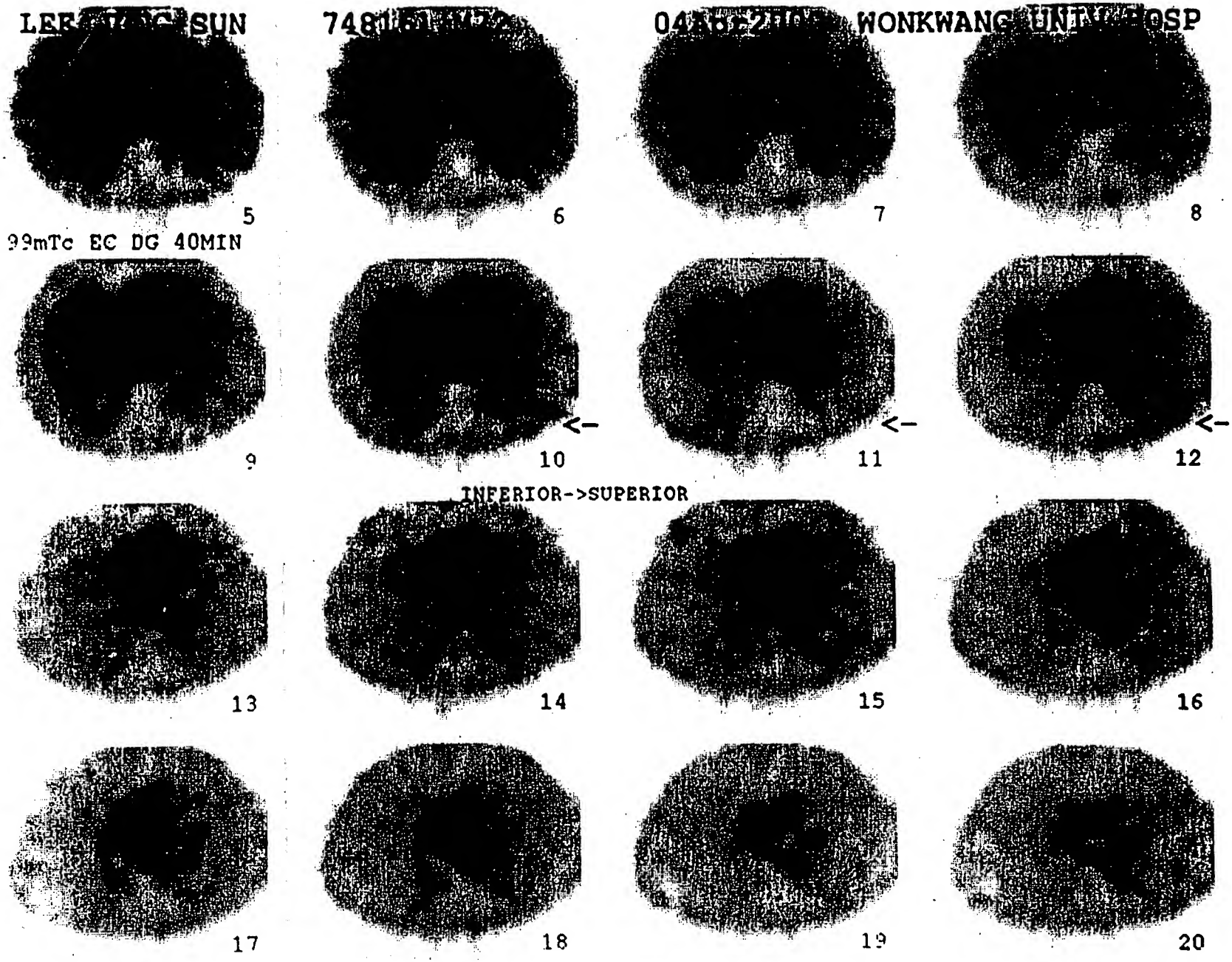
Dx: Pul.nodule (only necrotic material on biopsy)

TB pleurisy



09509152.062100

FIG. 85A CT of a patient with TB in lung.



0959152.062100

FIG. 85B SPECT with ^{99m}Tc-EC-DG of a patient with TB showed no focal

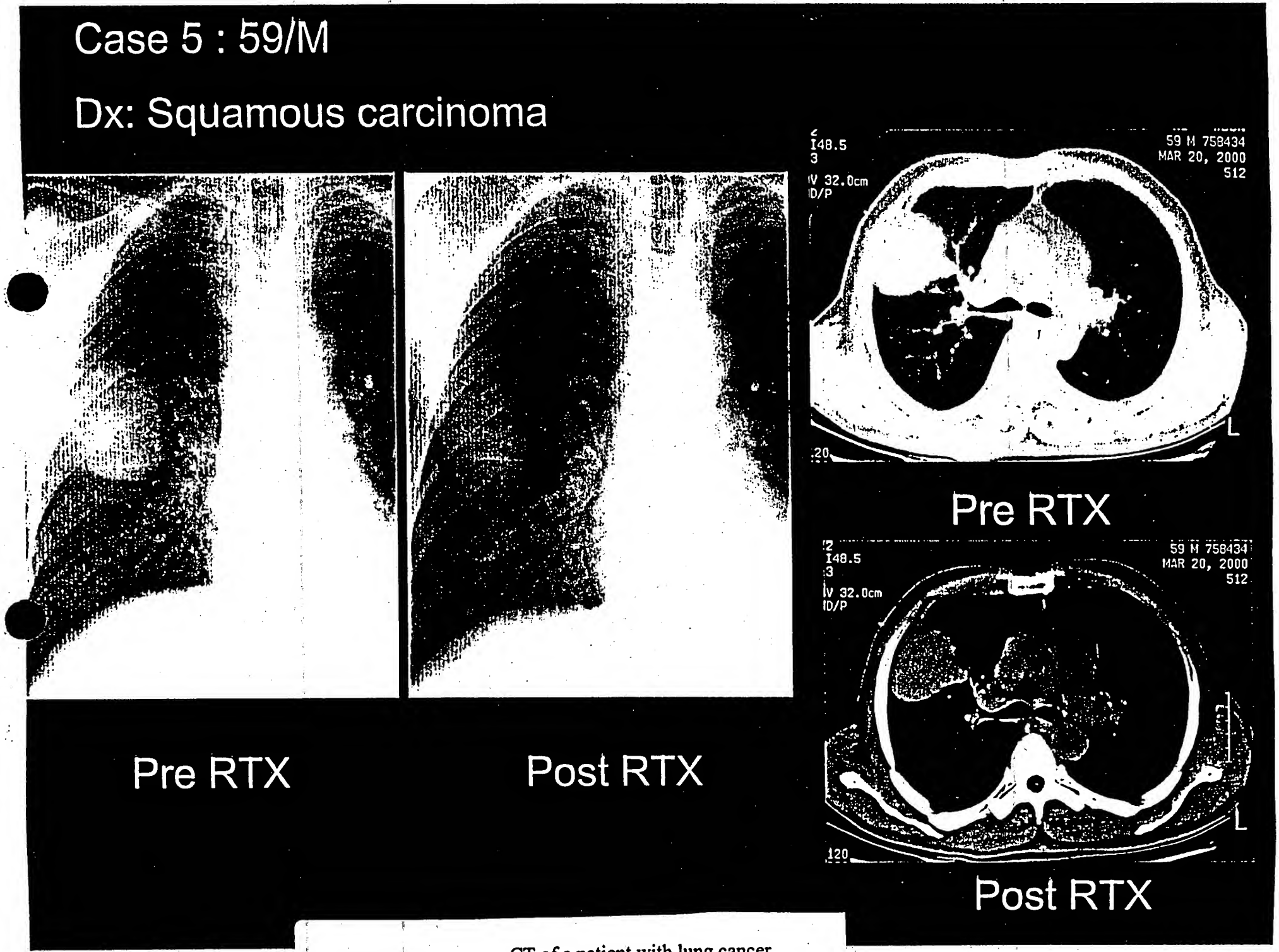


FIG. 86A CT of a patient with lung cancer.

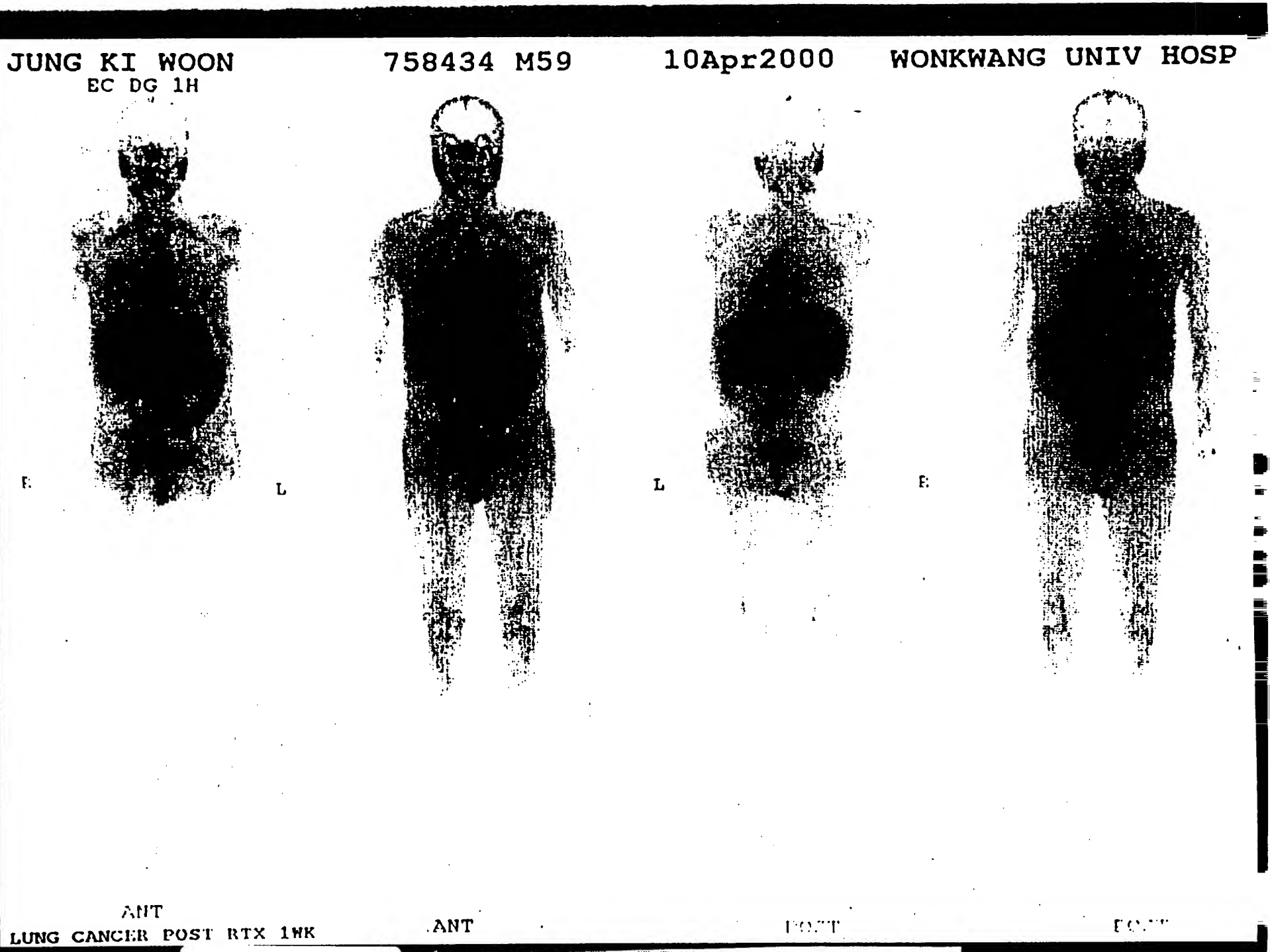


FIG. 86B Whole body images of ^{99m}Tc-EC-DG of a patient with lung cancer.

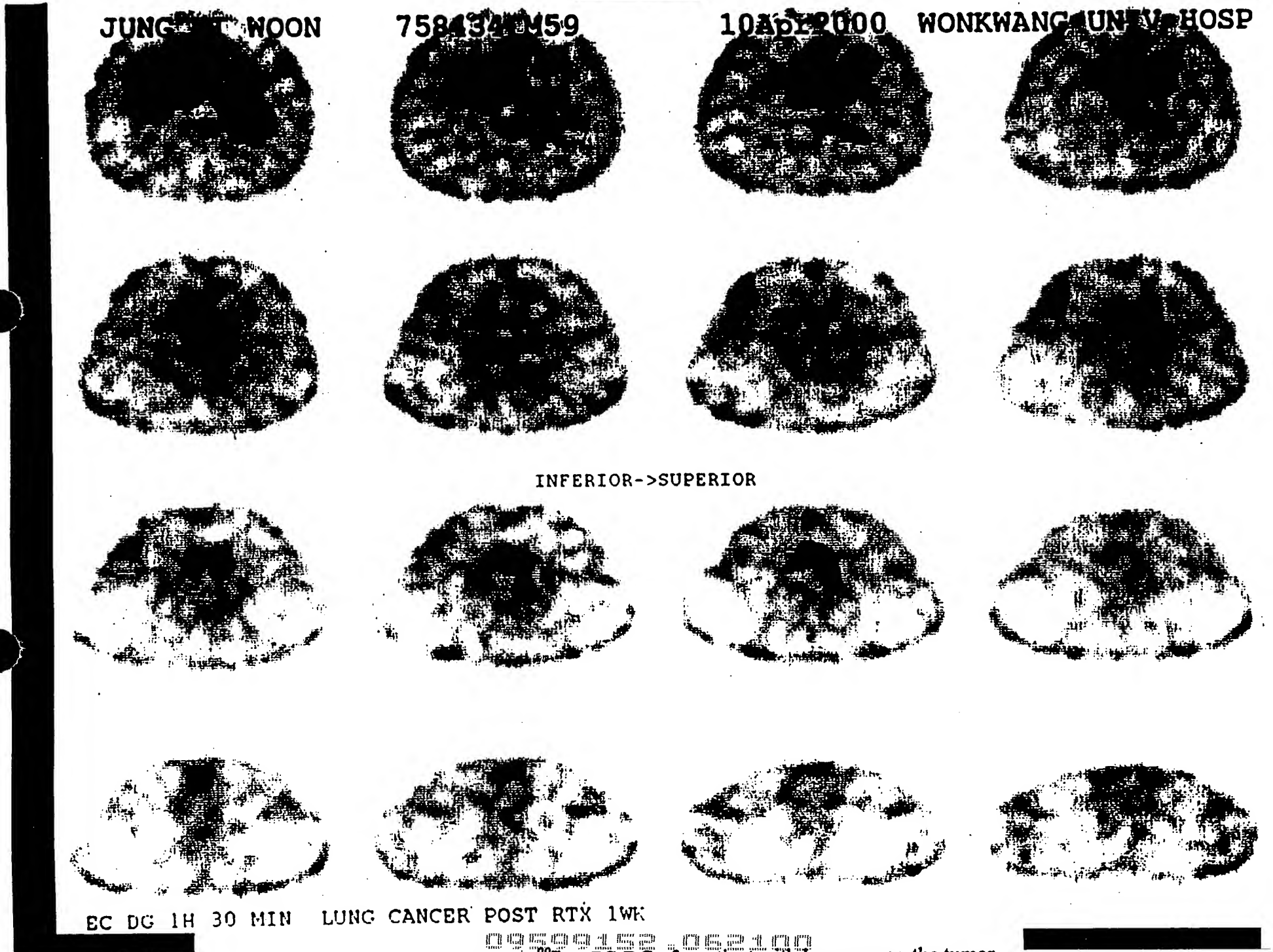


FIG. 86C SPECT with ^{99m}Tc-EC-DG of a patient with lung cancer, the tumor showed focal intensed uptake.